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VOL. II.—41ST YEAR SYDNEY, SATURDAY, DECEMBER 11, 1954 No. 24

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fourth patient

with anaemia

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(1) Batterman, R. C., Beck, G. J., and Lasser, G.: Am. Jour. Med. Sc., 214:268, Sept., 1947.
(2) Reznikoff, P., and Goebel, W. F.: Jour. Clin. Investigation, 16:547, July, 1937.
(3) Holly, G. R.: Bull. Univ. Minnesota Hosp., 20:475, Apr. 22, 1949.

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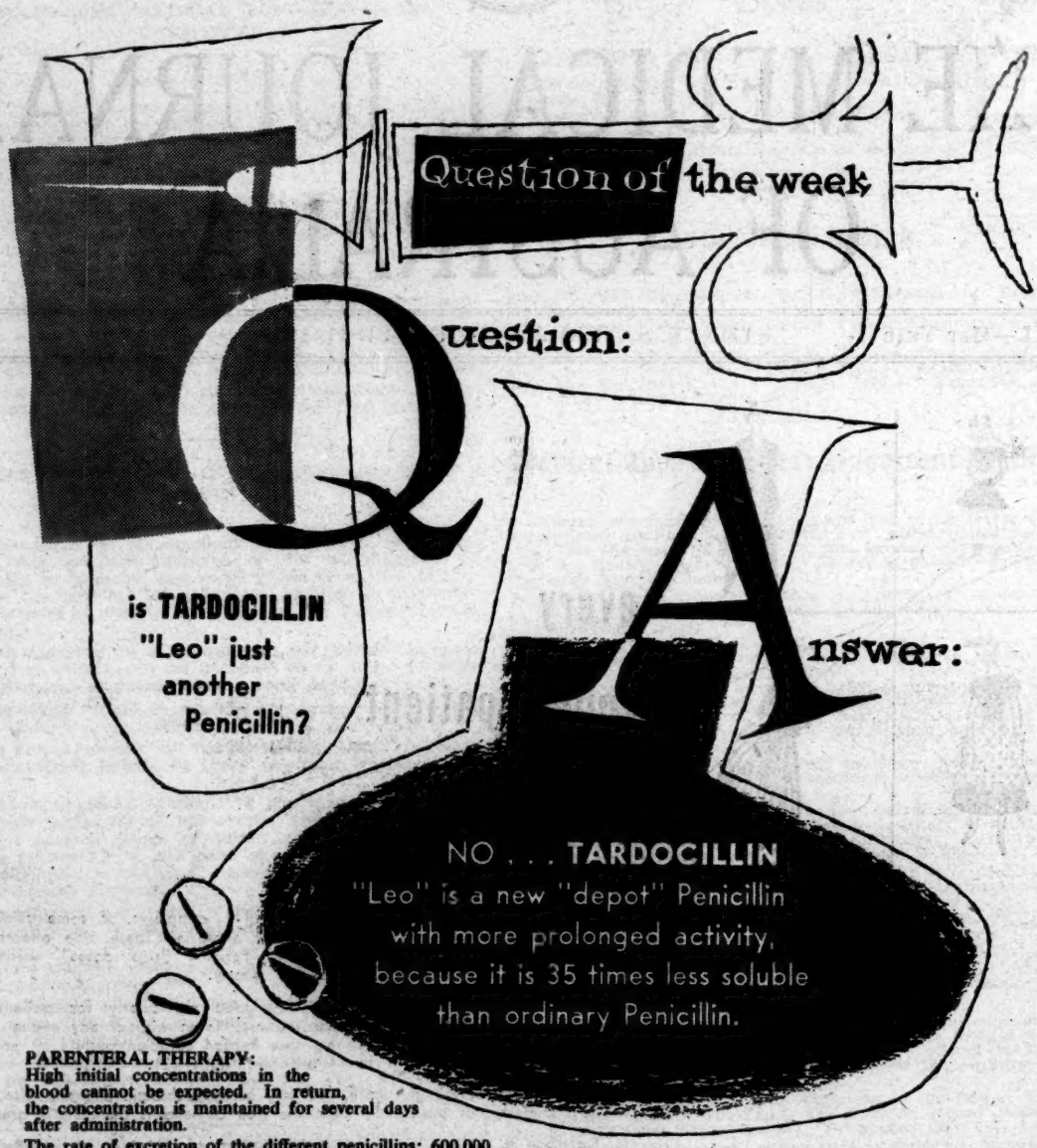
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FLUID AND ELECTROLYTE BALANCE.

By DONALD B. CHEEK, M.D.,

Children's Hospital Research Foundation, Cincinnati, Ohio, U.S.A.

SECTION I: THEORETICAL CONSIDERATIONS.

IN all aspects of medicine or surgery a sound knowledge of the behaviour of body fluids and electrolytes is essential. Whether a physician is dealing with œdema or metabolic disturbance, with acidosis, alkalosis or shock, or with dehydration, much of his therapeutic approach must be directed towards restoration of electrolyte and water balance. Ignorance of physiological principles will cost the physician lives and will jeopardize the results of the finest surgical skill. One leader in this field states that "probably the proper use of water and electrolyte solutions is responsible for saving more lives of seriously ill patients than is the use of any other group of substances".

It is true that the progress accomplished has been substantial in the last fifteen years, and it is becoming increasingly obvious that if the best is to be done for the patient, a consultant at all large centres must be available. There are always some willing to continue the management of the sick with unchanging patterns over the years—and with very stable mortality rates.

This manuscript deals with conditions pertaining to states of altered electrolyte and water balance, the information having been gleaned almost entirely from the work of other investigators. It has been written with the maximum brevity and simplicity so as to present facts rather than theory, and to attempt to produce a composite picture. Practical working hypotheses are put forward in preference to detailed discussions on controversial subjects. Information of value to the clinician and pediatrician in the field is given, but a physiological basis is emphasized.

To study the chemical anatomy of the body fluids, the unit that represents chemical equivalence is the milliequivalent. It therefore allows rapid comparison or easy detection of change in body fluid composition and of alteration in acid-base balance. Simple and logical thinking is always to be desired, hence the universal acceptance of this term. Milliequivalents are calculated as follows:

$$\frac{\text{milligrammes per litre}}{\text{atomic weight}} \times \text{valency} = \text{milliequivalents (per litre)}.$$

The normal values for plasma electrolytes are set out below in milliequivalents per litre of plasma.

Cations.		Anions.	
Na	= 142	HCO_3	= 24
K	= 5	Cl	= 106
Mg	= 3	SO_4, PO_4	= 3
Ca	= 5	Protein	= 16
		Organic Acid	= 6
	155		155

Another unit of concentration is the milliosmol:

$$\frac{\text{milligrammes per litre}}{\text{atomic weight}} \text{ (valency is disregarded).}$$

That is to say, this term expresses total particulate concentration (or number of particles irrespective of whether they be ions or molecules). This term is useful when one is thinking in terms of osmotic pressure. The serum contains approximately 300 milliosmols per litre.

It has been thought that the *milieu intérieur* of Claude Bernard represents the composition of the sea around us as it was some eons ago. Indeed, the relative increase in the present-day mineral content of the sea offers one mode of prediction as to the genesis of what we know to be human life. The fact that animals gradually emerged from the sea, carrying with them their sea-water environment, was surely the major step forward in biological adaptation to land life (MacCallum, 1926). That such a step was closely associated with organ change is amply illustrated, phylogenetically speaking, by the increasing development and structure of the adrenal glands and the kidney. This observation is well known to the student of comparative anatomy, and although it has been realized that the convolutions of the frontal cortex parallel those of the adrenal cortex, the kidney alone stands as the hallmark of this biological achievement and of the adaptation to a terrestrial environment. We must regard this centurion of the homœostatic portal, composed of a galaxy of delicate and incredible units, as the major moderator, protector, discriminator, conservator and rejector of our salt and water environment. It is indeed strange that the kidney—so long regarded only as the organ for the excretion of waste products—should now find a place that reveals this latter role as being perhaps the least important. During the process of disease there is alteration of our cellular fluid environment which is usually the reflection of altered cell metabolism. Quite apart, then, from our immediate responsibilities, the study of water and electrolyte metabolism has told us much concerning disease, and in terms of J. L. Gamble (1951) we are beginning to draw aside the "gossamer curtain" and we are obtaining occasional glimpses of cellular behaviour.

Measurement of total body water in the adult reveals this to be in the region of 45% to 55% of body weight (Soberman *et alii*, 1949). Larger values (70% to 80%) obtain for infants and newborn babies (Friis-Hansen *et alii*, 1951). Katcher *et alii* (1953) have obtained results that indicate that from six weeks to eight months the total body water ranges from 710 to 550 cubic centimetres per kilogram. These results can be accurately obtained through the use of deuterium oxide or by Soberman's method in which antipyrine is used. According to Friis-Hansen *et alii* (1951), the total body water content (in litres) in children may be obtained from the body weight in kilograms by the following formula:

$$\text{total body water} = (0{\cdot}55 \times \text{body weight}) + 0{\cdot}51.$$

We can therefore regard the human organism as being made up of water *plus* cell mass with fat as a variable quantity containing no water. Except in young infants the greatest proportion of body water lies within the cell. In the newborn infant almost 50% of the total body water may be present outside the cell; but as age progresses extracellular water diminishes (Cheek, 1954c). This extracellular water is made up of two main compartments which yield a continuous phase with respect to free and rapid ionic exchange. These two compartments are the vascular space or blood volume, and the interstitial space, which contains the vital fluids and lymph that flow across and around the cells, and like the sea from which it has been derived, it is subject to mild ebb and flow.

Let us consider for a moment the vascular compartment of the extracellular phase.

Because the endothelial walls of this compartment are not readily permeable to protein, the osmotic pressure of the plasma is a little higher than that of the surrounding interstitial fluid. The two media are in a constant state of dynamic exchange and flux. It has long been recognized that protein plays a prominent role in the maintenance of plasma volume, hence its priority over saline in the treatment of incipient shock. In terminal capillaries the hydrostatic pressure at the proximal end accelerates the passage of fluid into the interstitial space; yet a little further along the plasma protein by exerting its oncotic effect (oncotic pressure) hastens the return of fluid. Alternatively the interstitial fluid becomes part of the active lymphatic flow and eventually joins the venous system via the thoracic duct. In the minor and major circulations such as these, the intermittent exchange of nutrient and vital substances, waste products of metabolism, vitamins and hormones has been accomplished. The fluid surrounding and within the vascular compartment, the osmotic, oncotic and hydrostatic pressure, all support the plasma volume, while the left ventricular beat circulates the all-important carriers of oxyhæmoglobin. The concept of fluid circulating from the terminal capillaries is in accord with Starling's classical hypothesis. It has been shown with improved methods that just as much plasma protein is to be found outside the vascular system as within it. Since interstitial fluid is thought to contain less protein (but more than 0·5%) there must be an effective gradient between the interstitial fluid and the body cells as well as between the vascular space and the tissue fluids. Recent investigations with the use of labelled proteins (Drinker, 1946) have informed us that protein can pass through capillary walls more readily than we have suspected. These remarks apply particularly to the terminal capillaries or sinusoids of the liver and spleen, where easy passage of protein occurs (Landis, 1946; Forker *et alii*, 1952). This pathway leads either through the cytoplasm of the cell or via the intercellular cement substance of the capillary wall. Protein is in a state of progressive and dynamic equilibrium. When there is protein deficiency or a low serum albumin content, there is some breakdown in oncotic and osmotic relationships. Sodium and water tend to accumulate in the interstitial fluid, as Weech demonstrated twenty years ago by animal experiment (Weech, Goettsch and Reeves, 1936). Very little information has been added in this direction since then. We have still much to learn concerning the behaviour of protein.

The Extracellular Fluid.

By physiological extracellular fluid we mean that phase of body fluids that lies outside the cellular mass and with which the body chloride is in equilibrium. Actually, some of the extracellular fluid is really in the form of a colloidal "gel". This need not disturb the thinking. The plasma, the cerebro-spinal fluid, the lymphatic and joint fluid, and the aqueous humour are, perhaps, the only true liquids in the extracellular compartment. It is of importance to be able to obtain information concerning the extent of extracellular fluid volume changes. This need for information does not merely rest on the assessment of dehydration or œdema, but rather it affords us a means of detecting alteration in cellular composition and of departures from normal acid-base balance. For it can be seen that if changes in extracellular fluid and electrolyte can be measured, then, provided intake and loss are accounted for, movement of electrolyte into or out of cells can be revealed. Furthermore, since the total electrolyte content equals the volume of distribution multiplied by the concentration, and since chloride is nearly all extracellular, we can at once determine whether a low chloride concentration means chloride deficiency or not.

There is as yet no substance that will measure with precision extracellular water. Numerous agents have been proposed, but only two will be considered here. Briefly, when we are thinking of any substance that will measure this phase, certain criteria must be fulfilled. Such a substance should not be metabolized, should not sequestrate in bone or elsewhere, and preferably should be excreted slowly, yet reach equilibrium rapidly when once inside the body. Inulin, which represents a complex carbohydrate, adequately fulfils most of these criteria. However, it is fairly rapidly excreted, and it is necessary to use a constant infusion pump for administration. It does not reach rapid equilibrium and is unsatisfactory in œdema. In addition to this, the inulin molecule slowly penetrates

the fibrous and connective tissues which lie in the extracellular phase and which contain chloride. The value obtained for adults (16% of body weight) is smaller than the true extracellular space. For children aged from six weeks to eight months, a mean value of 265 cubic centimetres per kilogram has been obtained (Katcher *et alii*, 1952). Chloride lies in the connective tissues of the extracellular phase, and possibly some of it is not in ionic equilibrium. In addition to this, some chloride also is to be found inside the cells. Muscle cells, for instance, which contain about 70% of the body's intracellular water, contain chloride at a concentration of four milliequivalents per litre. Altogether it is not known how much chloride is intracellular. This value probably does not exceed 10%. When we have determined that amount of chloride that

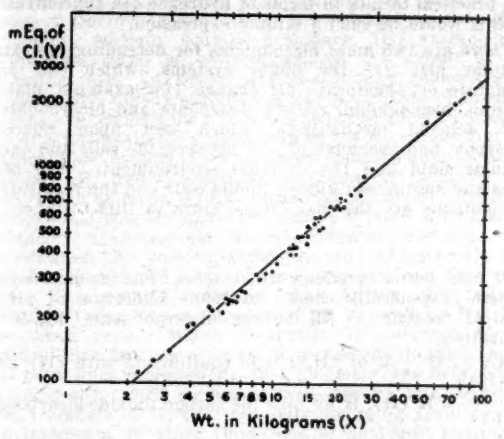

FIGURE I.

The total body chloride of 50 normal infants and children (aged two weeks to fifteen years) plotted against body weight in kilograms on a log graph. The linear relationship is in accordance with the differential growth equation $y = bx^k$, where y = total body electrolyte and x = body weight and b and k are constants. Some adult values have been included. (After Cheek, *Pediatrics*, July, 1954.)

lies within the cells of the body, it will be possible to define an extracellular space that is morphologically and biochemically acceptable. The nearest approach to this problem has been made recently by Nicols and Wallace (1953). These workers have shown that after twenty-four hours, analysis shows that nephrectomized dogs which have received inulin have an equal distribution of body chloride and inulin, provided one corrects the chloride space for chloride which is incorporated in the connective tissues at a high concentration. It would seem that inulin, which is rapidly excreted, and diffuses too slowly, is an unsatisfactory agent, and that the corrected chloride space is the logical measurement to pursue. Isotopes of chloride (by estimation of their volume of distribution) can be utilized to define the chloride space (Threefoot, Burch and Ray, 1953). I have approached the problem by using bromide and by adapting one of the methods of Conway for serum assay (Cheek, 1953). This substance conforms to all the criteria, except that like chloride it penetrates the cells to a slight extent. Fortunately the chloride space is very similar to the bromide space, and the latter ion is distributed in a similar ratio to chloride. Indeed, the volume of distribution of bromide multiplied by the serum chloride concentration is an accurate measure of total body chloride, and I have used this to measure total body chloride in children (Cheek, 1954*a*, *b*, *c*). If correction is made for the entrance of bromide into red cells, an extracellular space for young adults of 20% to 21% is obtained. In infants this space represents 35% of the body weight. An index of extracellular water can be obtained concomitantly with an accurate measure of total body chloride. This method, which is relatively simple, presents a reasonable approach to the problem.

From the graph in Figure II (to be mentioned presently) we can predict the extracellular volume in litres at different body weights (in kilograms) during growth.

From birth to the weight of eight kilograms, extracellular water (E_1) will be calculated as follows:

$$E_1 = (\text{body weight} \times 0{\cdot}233) + 0{\cdot}380.$$

From eight to 30 kilograms, extracellular water in litres E_2 will be calculated as follows:

$$E_2 = (\text{body weight} \times 0{\cdot}24) + 0{\cdot}300.$$

These equations take into consideration the fact that chloride is mainly extracellular and represents the chloride space corrected for Donnan equilibrium, serum water content and the red cell chloride content.

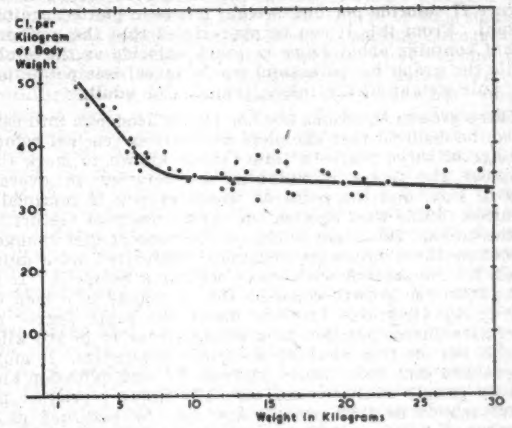

FIGURE II.

Total body chloride per kilogram plotted against body weight in kilograms. Note rapid fall in chloride during the first year of life. This reflects the large salt reserve of the infant. As chloride is mainly extracellular, we can predict the approximate volumes of extracellular fluid during growth. (After Cheek, *Pediatrics*, July, 1954.)

In summary then, approximately 10% of the body weight represents the vascular space, 35% (vascular *plus* interstitial) equals the total extracellular phase in young infants, and this diminishes progressively with age to about 20% for adults. Intracellular water in the infant tends to approximate in volume the extracellular water. In the adult intracellular water is calculated to be in the region of 35% of the body weight. Since fat is penetrated poorly by water, but accounts for body weight, obviously fat hinders one from expressing or measuring body compartments in terms of percentage of body weight. Hence, it would be ideal to express body water or electrolyte in terms of lean body mass or "fat free body". This averages 73% of the total body weight. Total water is a function of lean body mass, and Pace (1945) has shown in animals

$$\text{that } \frac{\text{total water (litres)}}{0{\cdot}732} = \text{lean body mass in kilograms.}$$

Extracellular water appears to be the best reference point when metabolic measurements are being made (Wedgewood *et alii*, 1953).

The Distribution of Electrolyte.

We have dealt with the distribution of body water, making brief allusion also to the distribution of protein. We must now consider electrolytes. Chloride, as already stated, is mainly extracellular, and it is particularly rich in the skin. Chloride also resides in the collagen and in cartilage. At least 15% or more of body sodium is in the bone. Not all bone sodium is in equilibrium with body fluid, and not all is readily available for metabolism; 12% of sodium is intracellular, while the rest resides mainly in

the extracellular fluid. By contrast, potassium is almost entirely intracellular and some is here combined with protein. Forbes (1952) and previous workers have given us a much clearer picture of the relationship between growth and electrolyte content. The total body content of sodium, potassium and water follows the differential growth equation, which can be written in the general form $y = bx^k$, where y = weight of a particular organ (or sodium, potassium or chloride), and x is the weight of the body; k and b are constants. By logarithms, this equation gives a linear relationship. The logarithm of weight plotted against the logarithm of total body sodium, for example, would yield a straight line. In the diagram presented (Figure I) it has been found that chloride also conforms to this relationship. Here total chloride in milliequivalents is plotted against body weight from birth to adolescence. Some adult values have been included. In Figure II chloride per unit weight has been plotted against weight. From this it can be appreciated that the newborn infant contains about twice as much chloride as the adult, while the graph for potassium would reveal less potassium per unit weight in the infant than in the adult.

These growth equations are not just of academic interest; it can be deduced that chemical maturity is reached before the age of three years—a time that is known to mark the "end of the phase of infantile deceleration in overall growth rate, and the point at which growth is minimal". Moulton (1923) first applied the term "chemical maturity" to the human. He meant to convey the concept that changes in composition, following "chemical maturity" were quite small by comparison with those occurring before it. It is clear from the growth equation that a change in a man of one to 10 kilograms involves about the same degree of alteration in composition as a change from 10 to 100 kilograms, but the time element is entirely dissimilar. It must be realized that body tissues increase by multiplication and not by simple addition, and virtually never reproduce an exact replica as they grow. Age may be regarded as a process of "drying out", or one of "desalting"; but this aging process is fastest when we are young. From a chemical viewpoint we can predict the composition of growing tissue. It is of interest to realize that available data suggest that the ratio of total sodium to chloride in the infant and in the adult is approximately the same (Gamble, 1954) and similar to the ratio of sodium to chloride in the serum. I have already emphasized that their locations in the body are dissimilar.

Cell Electrolyte Structure.

The differences between the composition of extracellular and intracellular fluid are striking. The major extracellular cation is sodium (making up about 90% of the osmotic base), and the major anion is chloride. This is in contrast to the intracellular ascendancy of the cation potassium and its major anion phosphate. Chloride remains chiefly extracellular. Intracellular sodium can move out quite freely into the extracellular compartment. Since chloride is restricted to the extracellular fluid, a transfer of intracellular sodium to the extracellular fluid will result in an increase of sodium bicarbonate, and likewise a transfer of sodium into the cell will produce a reduction of bicarbonate. Such changes will alter extracellular pH values and the distribution of body water. In certain pathological states extracellular sodium will exchange for intracellular potassium, and such a transfer of ions may be considerable; the appreciation of this "sodium shift" is most important in assessing the mechanism necessary to maintain the serum pH. We owe our understanding of this dynamic state to the work of Darrow, who disproved the hypothesis that potassium was fixed inside the cells. The dissimilar distribution of electrolyte between intracellular and extracellular fluids draws attention to the mystifying and inherent characteristics of the cell membrane. We believe that the osmolar concentrations on either side of the cell membrane are equal. We do not know how these dissimilar concentration gradients for sodium and potassium are maintained.

Although we shall later discuss alterations of electrolyte in disease, deficits of potassium or of chloride usually lead to alteration of cellular sodium. In many instances an aberration of cell electrolyte structure is reflected in the composition of the extracellular fluid or in the plasma water. It should be noted that this equality of osmolar concentration on both sides of the cell membrane may apply only under certain conditions.[1] Cell osmotic activity probably varies with cell metabolism (Conway and Fitzgerald, 1942).

Acid-Base Balance and pH.

The pH is defined as the logarithm of the reciprocal of the hydrogen ion concentration $\left(\text{pH} = \log \frac{1}{(H^+)}\right)$. It is not practical to talk in terms of hydrogen ion concentration as this would be such a minute expression.

There are two main mechanisms for defending the extracellular pH: (i) the buffer systems, which can only moderate or ameliorate pH change (for example, plasma protein, hæmoglobin, citrate, phosphate and bicarbonate); (ii) delayed mechanisms, which rest upon selective transport and exchange of ions between the cells and extracellular fluid and the external environment. The body cells and specialized kidney tubule cells and the respiratory mechanisms are the main moderators in this instance.

Buffers.

Of the buffer systems, the carbon dioxide-bicarbonate system is generally chosen to define alteration of pH in clinical medicine. All buffers undergo some degree of ionization.

$HA \rightleftharpoons H^+ + A^-$ or (HA) is in equilibrium with (H) (A), or $\frac{(HA)}{(A)} = K\,(H)$. If we take the carbon dioxide-bicarbonate system and apply the law of mass action, we can express the pH thus (taking logarithms): $\text{pH} = K + \log \frac{BHCO_3}{H_2CO_3}$, where K is a constant = 6·1. This is known as the Henderson Hasselbalch equation.

The normal extracellular pH lies between 7·35 and 7·45. Below 7·35 we have a state of acidosis, and above 7·45 alkalosis is present. The ratio $BHCO_3 : H_2CO_3$ is 20:1. Hence, it can be appreciated that large changes in the bicarbonate content of the blood can be readily counteracted by a small change in the dissolved carbonic acid, and since the dissolved carbon dioxide in the blood is in equilibrium with the carbon dioxide tension in the lungs, the respiratory mechanism which is sensitive to changes in carbon dioxide tension and pH can, therefore, adjust and counter to a significant extent alteration in acid-base balance. One must not forget that it is the ratio of $BHCO_3$ to H_2CO_3 that is important in defining pH, and not the absolute amounts. In metabolic acidosis we usually find an increased respiratory rate, while in metabolic alkalosis hypopnœa may be seen.

The change of oxyhæmoglobin to reduced hæmoglobin permits the conveyance of considerable amounts of carbon dioxide to its portal of exit without undue change in the pH. Plasma protein, by virtue of its amino and carboxyl group, also acts as a buffer, and the phosphate system of buffers is of considerable importance in the kidney. The excretion of dihydrogen phosphate in preference to disodium phosphate effects a loss of H ion and a return of Na^+ to the body. The buffers, by varying their degree of dissociation or ionization or by taking up or liberating H^+, tend to reduce departures from the normal pH but never can completely compensate for such changes. The pH of body cells is lower than that of extracellular fluid; it is probably in the region of 6·75.

[1] Investigations in progress present evidence indicating that osmolar concentrations on either side of the cell membrane are equal in water intoxication.

Cell Adjustments to Change in Extracellular pH.

Ions that are not readily metabolized or volatilized are termed "fixed". Na^+ and K^+ represent fixed cations, and Cl^- is spoken of as fixed anion. The amount of bicarbonate present is equal to the difference between the amount of fixed cation (Na^+ and K^+) and the amount of fixed anion (Cl^- principally). Bicarbonate is by no means fixed, and fluctuations in the relative amounts of fixed anion and fixed cation will produce changes in the bicarbonate, and, therefore, would alter pH if the respiratory mechanism was not invoked. Furthermore, the total amount of intracellular sodium is approximately equal to the total amount of extracellular bicarbonate. Hence, when a sodium shift occurs into the cells (for example, loading of an experimental animal with sodium bicarbonate), a transfer of sodium into the cell reduces the extracellular bicarbonate, and therefore obviates to some extent the potential pH change. Darrow *et alii* (1948) showed that in potassium deficiency, without sodium deficiency, the extracellular bicarbonate could be equated against the extent of cell potassium loss. A linear relationship was demonstrated. Cooke *et alii* (1953) studied cellular electrolyte changes in respiratory acidosis, and they were able to show by making use of other available animal data in the literature that the intracellular sodium bore a linear relationship to extracellular pH, under conditions of metabolic acidosis and respiratory acidosis, and in metabolic alkalosis. Darrow's group and Cooke *et alii* (1952) also studied a single ion deficiency of potassium in experimental animals. We investigated the possible renal and cell adjustments that would be occasioned by potassium deficiency and its correction. The results indicated that during the induced alkalosis there was a transfer of H^+ as well as Na^+ into the tissue cells. When eventually H^+ returned to the extracellular fluid as a result of potassium therapy and of cell potassium replacement, this alkalosis was neutralized. Orloff *et alii* (1953) confirmed these results, and suggested that transfers of H ions into cells including renal tubules are important in other conditions of acid-base imbalance.

It can be appreciated, without going into further detail, that such mechanisms as these leave the ordinary buffer systems behind as secondary. These relationships emphasize that the treatment of acidosis or alkalosis by the administration of calculated amounts of acid or alkaline salt is often quite unscientific and of questionable value. Instead, one should give appropriate electrolyte with a view to cell repair. Further, the present work reveals our ultimate aim of treating fluid and electrolyte problems from the viewpoint of changes in cell composition, for cell composition is intimately related to acid-base balance and normal health. Nitrogen retention and growth are not compatible with aberrant cell composition (Muntwyler, 1953; Cannon, 1952).

The Role of the Kidney in Acid-Base Regulation.

Our present concepts of kidney function will be briefly reviewed presently; suffice it to say here that important ionic exchanges take place in the kidney tubules. The amount of reabsorption or, more properly, ionic transport depends on several factors. Hence, it will be realized that differential amounts of fixed anion and cation that eventually are selectively reabsorbed from, or excreted into, the urine will influence the pH of the plasma. This selection is such as to maintain a normal pH. To quote one example, mercurial diuretics cause a greater relative loss of chloride than of sodium, hence alkalosis can be produced. Furthermore, the work of Pitts (1950) has revealed that the kidney tubules can actively excrete H^+, so that fixed anion can be excreted with H^+, and fixed cation such as Na^+ or K^+ can be returned to the body. But a more important mechanism, although a little slow to be initiated, is the conservation of fixed base by the ammonia mechanism. The kidney can readily form ammonia from glutamine. The NH_4 ion is thus available for combination with an anion ready for excretion. By the same token, the kidney can readily conserve anion by the excretion of bicarbonate for, say, chloride. It is important to provide the kidney with adequate water so that proper control of electrolytes can be effected. The kidney is continually rebuilding the extracellular fluid, continually effecting the escape of unwanted anion, yet usually yielding a conservation of cation, especially sodium; for sodium, as was mentioned previously, is fixed and determines the osmotic base, any fall producing a reduction of osmolar concentration or any increase leading to an increase in total ions. The adrenal gland assists the kidney with the body's conservation of sodium.

In summary, then, with respect to all the mechanisms that have briefly and inadequately been referred to, the kidney provides the foundation for homœostatic defence.

Kidney Function.

The school of Homer Smith has given us a concept of renal function (1951) that has been widely accepted and criticized. This concept may in the course of time undergo considerable modification. The fluid passing through the glomerulus is essentially an ultrafiltrate of plasma containing at the most 20 milligrammes of protein per 100 millilitres. As the fluid passes down the first tubular segment (the proximal tubule), 80% of sodium ion is reabsorbed actively—that is, energy is required for the tubule cells to carry out this selective retention. As a result, the fluid in the proximal tubule would be rendered hypotonic in comparison to the peritubular fluid, if it were not that water is reabsorbed passively; and by the time the tubular fluid reaches the thin segment it is still isotonic. The passive reabsorption of water is known as "obligatory water reabsorption". Therefore, some 80% of electrolyte and water has been returned to the body, and under normal circumstances this amount is thought to be reasonably fixed. As we pass into the distal tubular system we cannot be so sure of our ground. Of the reduced volume of fluid entering this tubular system, the reabsorption of water and that of sodium are thought to be active processes and not necessarily interdependent. The active reabsorption of water is termed "facultative reabsorption". It is dependent on the body's need and is directed by the antidiuretic hormone from the pituitary.

With respect to sodium, Homer Smith believes that there is a maximum amount per unit time that can be transported through the distal tubular cells to the peritubular fluid. (This is technically referred to as the "distal Na Tm" or the maximal sodium transport.) Since a fixed amount of sodium is reabsorbed in the proximal tubule system, the appearance of sodium in the urine will depend on the amount of sodium presented to the distal tubular system per unit time. If this exceeds the distal Na Tm, sodium will be excreted; if not, then very little will appear in the urine. Now the amount of sodium that presents to the kidney tubule depends on the rate of glomerular filtration and on the concentration of sodium in this filtrate. These two factors define the sodium load. If either the sodium concentration in the plasma or the glomerular filtration rate increases, then the sodium load also increases and a greater sodium load reaches the distal tubule, and this load may exceed the amount of sodium that can be transported. If this is so, sodium will appear freely in the urine. In sodium depletion one might expect to find a greatly diminished filtration rate. This is so only in the experimental animal with acute sodium depletion. In chronic sodium deficiency, filtration rate is normal with polydipsia and polyuria (Cizek and Huang, 1951). One must state at this juncture that variation of glomerular filtration may not be so important in determining sodium excretion. This is where other workers have taken issue with Homer Smith; for ample evidence exists to show that active alterations of tubular reabsorption are of greater moment than variation in glomerular filtration rate (Wiggins *et alii*, 1951; Green *et alii*, 1951; Mueller *et alii*, 1951). It would seem, therefore, that it may not be possible to define a distal Na Tm; indeed, the reabsorption of sodium in the distal tubule may well be subject to the body's need, and under the control of influences from the adrenal-pituitary axis and/or subject to neural control.

Rapaport, Brodsky, West and Mackler (1949) have shown that, under conditions of water restriction, there is a definite relationship between the urine flow (volume per unit time) and the rate of total solute excretion. This can be conveniently demonstrated by the infusion of any solute such as urea, glucose, electrolyte or mannitol. The same curve is always obtained and is independent of the rate of glomerular filtration and of the mechanism of excretion. It matters not whether the substance is filtered and reabsorbed, or whether it is actively secreted by the tubules; the same curve pertains under hydropenic conditions. In Figure III we see this curve in each of the four graphs. The upper limiting line represents the total solute concentration of the urine, and the shaded areas, the relative concentrations of the various solutes during

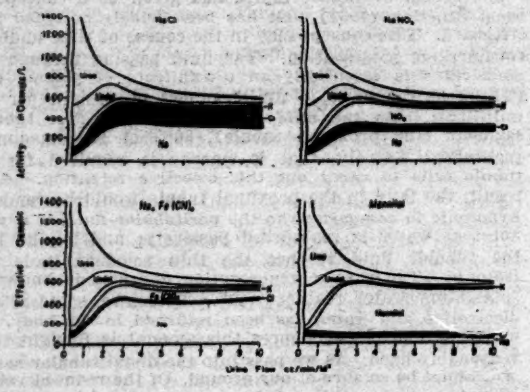

FIGURE III.
Patterns of urine composition during osmotic diuresis in hydropenic dogs. (By courtesy of Dr. Clark D. West.)
For explanation see text.

loading. The total solute concentration of the urine bears a fixed relation to the flow, and this relationship is independent of the nature of the solutes composing the urine. The greater the rate of solute excretion, the higher the urine flow, but the lower the concentration of any particular solute. One would predict from this curve that in the final portions of the nephron the total solutes are assembled for excretion, and in further passage only water is absorbed.

It is desirable for us to determine the exact mechanism and behaviour of sodium reabsorption in the distal tubule, as anomalies of this mechanism have been alluded to as being causatively related to œdematous states, cardiac failure, cirrhosis, eclampsia and other conditions.

It was shown by the classical experiments of Verney (1947) that osmoreceptors exist in the hypothalmus, and that increases in osmolarity augment the release of the anti-diuretic hormone from the posterior lobe of the pituitary. Hæmodilution effects a suppression of anti-diuretic hormone, and its influence on the distal tubule is absent. A hypotonic urine of large volume results. These findings have clarified much of our confusion, but we still have a substantial amount to learn regarding the action of anti-diuretic hormone, as its presence has been detected in conditions of electrolyte depletion with reduced osmolarity of the body fluids (Leaf, 1951). Moreover, the repeated injection of this hormone in the presence of progressive water loads will cause a decided, abrupt, and large sodium and chloride loss in the urine simultaneously with falling sodium and chloride levels in the plasma (Leaf *et alii*, 1953; Weston *et alii*, 1954). Working along these lines in conjunction with C. D. West, we have been able to reproduce this striking phenomenon in dogs. This chloruresis is related to a hypotonic expansion of the extracellular fluid, and is probably not related to the effects of pitressin *per se*. The circumstances invite the hypothesis that there is a volume receptor in the body which responds to increments in the interstitial or vascular compartments and gives rise to reduced sodium reabsorption in the kidney tubules. Preliminary experiments suggest that this paradoxical salt loss is dependent on an intact renal autonomic nerve supply. Removal of the renal nerves sometime prior to water loading prevents this phenomenon. Factors which augment the expansion of extracellular fluid, such as ACTH or desoxycorticosterone, serve only to augment the rate of salt loss and eventually to render the animal even more salt-depleted. A volume receptor would be one more modifying influence on sodium and water excretion. It is becoming increasingly apparent, then, that quite apart from the existing rate of glomerular filtration, an expansion of extracellular water can influence and reduce sodium reabsorption in the kidney tubules. It seems also that certain thoracic loci are sensitive to changes in venous pressure and when stimulated can give rise to water diuresis (Gauer *et alii*, 1954).

From what has been stated, it can be appreciated that much is known, but a great deal remains to be elucidated, and it is only now that the interrelation of these mechanisms is becoming clear.

In summary, then, we can state that of 170 litres of glomerular filtrate passing through the kidney each day over 80% is reabsorbed proximally. Alteration of glomerular filtration rate and/or changes in osmotic concentration may effect an increase or decrease in the sodium load which is presented to the distal kidney tubules. The resulting sodium retention or excretion, together with the existing osmolar concentration in the circulating fluids, influences the anti-diuretic hormone levels. Water conservation or excretion is the ultimate result. A return to normality in sodium and water balance is being continually effected in the presence of a disproportionate intake or an abnormal loss. Sodium excretion is also moderated by neural and hormonal mechanisms, and we are disinclined to believe that the glomerular filtration rate is of absolute importance in this respect.

Dehydration.

The symptoms and signs of dehydration are well known to every physician, and there is no point in restating them. The difference between hypotonic and hypertonic dehydration depends on the extent of salt loss relative to water loss. Hypertonic dehydration refers to a greater overall loss of water, and this deficit of water produces an elevation of serum sodium and of serum chloride and a somewhat uniform loss of fluid from both the intracellular and the extracellular compartments. As a result, this type of dehydration is easily detected clinically, and tissue turgor may reveal the tell-tale evidence at an early stage. There is a complaint of thirst on the part of the conscious patient, but in the unconscious state hypertonic dehydration is frequently overlooked. Indeed, unless maintenance requirements of fluid are carefully watched, this set of circumstances can be anticipated. Welt *et alii* (1952) have emphasized this danger. Hypotonic dehydration is a more usual finding and indicates a greater overall sodium loss. It can be readily occasioned in the infant by diarrhœa or vomiting treated in good faith by the mother with water but no salt. The sudden overall sodium loss produces a sharp reduction of plasma and extracellular osmolarity, with a resulting transfer of water to the cells. This state of increased cellular hydration was first demonstrated by the classical experiments of Darrow and Yannet (1935). There are shifts of water into the cells as well as external losses, and proportionately large deficits of extracellular water and of plasma water are occasioned. Shock is often impending. With the reduction of plasma volume there is a diminution in glomerular filtration and a rise in the blood non-protein nitrogen level. A reduction in cardiac output with hypotension and an increase in pulse rate, with a poor volume, are concomitant features. The apathetic or mentally confused adult, or the unconscious child with flaccid muscles, drawn face and sunken eyes, leaves no doubt as to the urgency of the situation. Sweating

may be noticed; perhaps this is related to the reduced osmolarity, but thirst is frequently absent in the conscious patient. We do not know how much of this symptomatology is due to extracellular losses and how much is due to increased cell hydration. In any event, the increase in cell hydration will not be large. As it is not always easy to replace large deficits of sodium in the adult by isotonic solutions, one would agree that the use of hypertonic saline (3%) is frequently desirable. In other words, with adults the problem should be attacked from the viewpoint of concentration deficits (to be discussed later).

For the moment we have been talking in terms of acute electrolyte or water loss, and it does not follow that chronic electrolyte depletion will reveal the same disturbances of physiology. Indeed, in states of potassium deficiency dehydration is mainly at the expense of cell water (for example, diabetic acidosis with coma). Although œdema is associated with a large expansion of extracellular water, the state of cell hydration is here influenced by the extracellular electrolyte concentration. Low plasma sodium levels may be associated with increased cell hydration, and under these circumstances shock and collapse can supervene, just as in hypotonic dehydration. Electrolyte is required. This set of circumstances is sometimes seen in cardiac patients receiving a very low sodium intake (Schwartz and Wallace, 1951). There is reason to believe that chronic electrolyte depletion augments the production of anti-diuretic hormone.

Metabolic Acidosis.

Metabolic acidosis is due to a relative or absolute decrease in the plasma sodium level. If, then, there is an increase of chloride relative to sodium, or if there is a sodium deficit without a chloride loss, metabolic acidosis results, and if the pH is below 7·35 an uncompensated acidotic state exists. Under these circumstances one can expect a shift of sodium from the cells to the extracellular fluid to offset the pH change. If acidosis and dehydration persist, one can anticipate a triple ion deficiency of sodium, potassium and chloride, and, as Darrow points out, potassium as well as sodium and chloride is necessary to restore normality.

Metabolic Alkalosis.

By contrast one would expect metabolic alkalosis to represent an overall increase in sodium relative to chloride. This is so. Under most circumstances a chloride loss without an equivalent amount of sodium, such as occurs in vomiting, produces metabolic alkalosis. I have mentioned previously that Darrow's group produced evidence to show that in uncomplicated potassium deficiency the metabolic alkalosis present is to some extent due to the transfer of H ion into the cells. This may occur concomitantly with the advantageous shift of sodium into the cells. Further and more recent work by Cooke, Segar, Reed and Darrow (in the press) indicates that there is a critical level of cell potassium. If deficits exceed this critical amount, metabolic alkalosis results. It can be deduced from their findings that metabolic alkalosis cannot be firmly established or sustained unless cell potassium deficiency exists. Thus, except for transient alkalosis produced by the injection of large amounts of sodium bicarbonate, the finding of a serum pH above 7·45 together with a raised bicarbonate level in the serum informs one of cell potassium deficiency and its replacement by sodium. The use of ammonium chloride for alkalosis, even though it tends momentarily to correct extracellular pH and may even ameliorate tetany, does not find a satisfactory physiological basis. Sodium chloride may fulfil extracellular deficits, but under these circumstances it also cannot make correction of intracellular change and may even exacerbate them. The replacement of the potassium ion has thus been emphasized.

Respiratory Acidosis and Alkalosis.

When the serum carbon dioxide tension becomes elevated owing to the unsatisfactory escape of this metabolite, we are dealing with respiratory acidosis. Injury or disease of the respiratory system commonly produces this change, and cyanosis is generally in evidence. Although the serum bicarbonate increases concomitantly with the increase in carbon dioxide, the concentration of the former is often insufficient, so that a pH change to the acid side is revealed. With the increased concentration of serum bicarbonate, that of chloride must fall if electrical neutrality is to be preserved. Presumably this task is undertaken by the kidney.

Respiratory alkalosis is accompanied by a decrease in carbon dioxide tension and results from over-breathing or from abnormal stimulation to the respiratory centre. It is commonly seen at high altitudes, in hysteria, and in salicylate poisoning. The serum bicarbonate and chloride concentrations are appropriately altered.

Section II: Practical Applications.

In the approach to electrolyte and fluid therapy, the régimes of D. C. Darrow, E. C. Pratt (Darrow and Pratt, 1952) and R. E. Cooke (Cooke and Crowley, 1951) have much to recommend them. A brief outline of the system and approach made in the Department of Pediatrics at the Yale University School of Medicine will therefore be set out; there are three general principles to be observed: (i) the correction of body deficits and the restoration of (a) electrolyte concentration and (b) volume of body fluids; (ii) maintenance therapy—the replacement of the usual physiological losses; (iii) contemporary replacement of abnormal loss—this, of course, includes persistent diarrhœa and vomiting, or loss from a fistula, renal salt-wasting, and so on.

The Correction of Body Deficits.

The first step in treating dehydration is a thorough evaluation of the clinical history and the completion of a thorough clinical examination. It is important to know whether the patient vomited twice before coming to the hospital or 20 times. It has been my experience not to find this important information in case histories. The nature of the vomitus is of little consequence, but some idea of the volume lost is of great help, for if vomiting has been continuous with only water replacement it is almost certain that hypotonic dehydration will be present and electrolyte must be given without delay. The concentration of potassium in the vomitus, for instance, can be five times the concentration in the plasma. If there has been vomiting without diarrhœa, one knows that chloride loss predominates (alkalosis), while diarrhœa alone produces an overall loss of extracellular sodium. Acidosis is to be anticipated. If possible one should always know what weight loss has occurred and during what period. One can at once assess to some degree the amount of electrolyte and water loss. An acute loss of 15% of body weight is a severe loss; 10% a moderate loss. It is quite illogical to proceed with biochemical investigations if one has not made full use of important evidence. The condition of the skin on examination, the inspection of membranes, the palpation of the fontanelle, a glance at the eyes and the skin surrounding them, the volume and rapidity of the pulse and the skin temperature in the extremities, all tell their own story. The study of the respiratory rate, depth of breathing and regularity of rhythm is never to be neglected. States of coma or tetany are medical emergencies. At this juncture one should be able to appraise the state of electrolyte and water balance, as to the approximate water loss and state of acid-base imbalance, and even as to whether hypotonic or hypertonic dehydration is present. The extent of these changes can be aided by biochemical investigation. Even here analysis of the blood will reveal concentration deficits only, with little or no help as to volume deficits (total amount = volume × concentration). Furthermore, it must not be forgotten that blood assay informs one of the status of the extracellular compartment, and only occasionally can one conclude that certain intracellular changes are present.

Of the laboratory aids, the most important are the serum sodium, chloride, non-protein nitrogen, potassium and bicarbonate levels, and pH. Hypotonic or hypertonic dehydration can be detected, and acidosis or alkalosis can

be exposed. However, the bicarbonate reading alone without the pH will not tell you whether you are dealing with respiratory acidosis or metabolic alkalosis. A useful rule to remember is that the chloride *plus* the bicarbonate *plus* 15 should equal approximately the plasma sodium level. A non-protein nitrogen estimation should always be made to evaluate renal impairment. A hæmatocrit value is also informative. Most modern hospitals possess, or should possess, a flame photometer of the internal standard type. Improved techniques enable one to determine sodium, potassium, chloride, carbon dioxide, pH, non-protein nitrogen and hæmatocrit values with from three to four cubic centimetres of blood. Besides the routine examination of the urine, one should determine the urinary pH with an appropriate indicator. The specific gravity is always indicative of the state of water balance, provided renal disease can be excluded.

Electrocardiographic recordings can be taken at once, and there are an inversion of the *T* waves and a prolongation of the *QRS* complex and depression of the *ST* segment in potassium deficiency and in hypocalcæmia. The actual or specific replacement of volume deficits will be discussed presently in greater detail under the various pathological conditions. Suffice it to point out here that the different proportions of electrolyte solutions and of water with glucose that are administered are not necessarily dependent on electrolyte findings. Previous experience, and the pattern of cell change known to occur in the condition under treatment, are of importance. However, gross departures from normal require prompt attention. A bicarbonate level of 10 milliequivalents per litre, if accompanied by a chloride value of 150 milliequivalents per litre, means that at least 80% of the initial replacement solutions should be glucose and water. Conversely, a chloride value of 70 milliequivalents per litre associated with a bicarbonate level of 10 milliequivalents per litre indicates severe electrolyte loss, hypo-osmolarity, and an urgent need for the continuous administration of electrolyte solution. The electrolyte losses are corrected according to the needs and deficits. For example, in gastro-enteritis with a 10% weight loss one knows that the body deficits are in the region of nine milliequivalents of sodium, nine milliequivalents of chloride, and 10 milliequivalents of potassium per kilogram of body weight. This can be replaced slowly in appropriate volumes of fluid (correction of volume deficits to be discussed separately).

We can make rapid partial corrections for losses of sodium and chloride by the injection of hypertonic solution. This brings us to a consideration of concentration deficits, which is more applicable to adults than to children. These losses can be satisfactorily and rapidly made good by the formula: Concentration desired *minus* concentration present multiplied by a distribution factor and body weight = milliequivalent required. $((Cd - Cp) \times fd \times BW = mEq.)$ For example, if the sodium concentration is 120 milliequivalents per litre in an adult weighing 50 kilograms and one wishes to restore this to normal: $(140 - 120) \times 4/10 \times 50 = 400$ milliequivalents of sodium required: that is, 890 cubic centimetres of 3% saline are required. The distribution factor under conditions of dehydration is 4/10 and is proportionate to body water and takes into consideration the concomitant changes of fluid volumes. It is usually not necessary to worry about concentration deficits except in severe sodium loss. However, a child with cardiac disease in a condition of "the low salt syndrome" through salt restriction and the exhibition of mercury may sometimes require such treatment as this. Likewise, in the collapse and heat prostration in fibrocystic disease, and perhaps occasionally in pink disease, partial correction can rapidly be made.

Maintenance Therapy.

In addition to fluid and electrolyte given to replace abnormal loss, the requirements due to urinary loss, metabolism, sweating and insensible water loss must be covered. This water requirement is calculated on the basis of Calories. We feed a child according to caloric requirements, and by the same token fluid requirement is a function of Calories metabolized. To make this régime uniform we can also measure electrolyte requirements in terms of caloric requirement. The problem is even more simplified by the fact that such a system will hold from birth to old age. If one's thinking is adjusted to this approach, a much more accurate appraisal of water requirement will be reached. After all, basal metabolism and water requirement are closely interwoven; measurement of insensible water loss in a baby provides a method for assessing the basal metabolic rate.

For all conditions at least 120 to 150 cubic centimetres per 100 (total) Calories metabolized are necessary, and during heat stress some 200 cubic centimetres or more are required. For insensible water loss 42 cubic centimetres of water per 100 Calories metabolized are lost. The urinary water loss is a function of the solute load and of tubular reabsorption. During starvation the water requirement is less, but with a protein-rich diet it is increased. These considerations are of importance, as during atmospheric heat maximal losses of water may occur as sweat and insensible water loss, and insufficient water may be available for the proper excretion of the nitrogenous products of metabolism. For this reason during heat stress babies should not be fed a protein-rich diet, as Cooke (1951) has demonstrated with scientific precision. Dilute fluids are preferable. The urinary solute concentration (specific gravity is a rough indication) varies with fluid intake, as has been represented graphically by Darrow and Pratt (1950).

To assess a child's water requirement we should take the basal caloric requirement (see Table I) and add 15% for specific dynamic action (diet), 5% for growth, 8% for each degree Fahrenheit of fever, and up to 100% for activity. The child will require 120 to 150 cubic centimetres for every 100 Calories. A child at rest in bed (and if ill) will obviously exhibit reduced activity (25%). Under usual circumstances, however, water requirements can be conveniently based on known total caloric requirements (for example, the neonatal infant metabolizes 110 Calories per kilogram). It is important to know how these amounts of fluid (120 to 150 per 100 Calories) are calculated. The patient will be kept in a satisfactory state of hydration with 120 to 150 cubic centimetres of water for every hundred Calories (total Calories) which are metabolized. The twenty-four hour urine volume at a convenient or desired specific gravity level together with the insensible water loss (42 cubic centimetres per 100 Calories) gives the water expenditure, excluding sweat and stool water. At a urinary specific gravity of 1012, 80 cubic centimetres per 100 Calories will be required for urine expenditure. To this add 42 cubic centimetres for insensible water loss and then 10 cubic centimetres for sweat and 10 cubic centimetres for stool water loss, so that one should administer about 140 cubic centimetres of fluid per 100 Calories metabolized. The following are examples.

1. In a one year old, 10 kilogram, fully active infant, the total caloric requirement is 100 Calories per kilogram, and the fluid requirement is $\frac{1000}{100}$ Calories $\times$ 140 = 1400 cubic centimetres.

2. In a 70 kilogram adult, metabolizing 2800 Calories, the fluid requirement is 3900 cubic centimetres (caloric expenditure, 40 Calories per kilogram).

More precisely we assess as follows the maintenance requirement of, say, a sick infant weighing nine kilograms with a temperature of 102° F.: basal metabolic rate, 500 Calories; 4° temperature elevation, 160 Calories; activity (25%), 125 Calories; specific dynamic action and growth (disregard here); total metabolism, 785 Calories. Water requirement, $7 \cdot 8 \times 140 = 1090$ cubic centimetres.

Under fasting conditions, when adequate glucose and water are being given, there is a protein-sparing effect, and urinary water loss falls by about 20 cubic centimetres per 100 Calories metabolized. The basal metabolism must be

assessed from height in obese or malnourished children. This régime, as proposed by Darrow, represents a rational and significant advance in our approach to fluid therapy.

Electrolyte Requirements.

The minimal daily needs are two to three milliequivalents of sodium and potassium and 1·5 to 2·0 milliequivalents of chloride per 100 Calories metabolized. For practical purposes about one-fifth to one-quarter of the fluid intake should represent isotonic electrolyte solution having a similar composition to extracellular fluid. This will cover maintenance requirements. Hence, in the previous example the electrolyte requirements will be as follows: sodium, 7·8 × 2·0 = 15 milliequivalents; chloride, 7·8 × 1·5 = 12 milliequivalents; potassium, 7·8 × 2·0 = 15 milliequivalents.

TABLE I.

Basal Metabolic Rate (Calories per Twenty-four Hours).[1]

Weight. (Kilograms.)	Girls.	Boys.
3·0	136	150
4·0	205	210
5·0	274	270
6·0	336	330
7·0	395	390
8·0	448	445
9·0	496	495
10·0	541	545
11·0	582	590
12·0	620	625
13·0	655	665
14·0	687	700
15·0	718	725
16·0	747	750
17·0	775	780
18·0	802	810
19·0	827	840
20·0	852	870
22·0	898	910
24·0	942	980
26·0	984	1070
28·0	1025	1100
30·0	1083	1140
34·0	1137	1230
38·0	1207	1305
42·0	1274	1370
46·0	1338	1430
50·0	1399	1485
54·0	1458	1555
58·0	1516	1600
62·0	1572	1660
66·0	1626	1725
70·0	1679	1785

[1] From F. B. Talbot, 1938.

Protein Requirements and Calories: The Protein-Sparing Effect of Glucose.

Two and a half grammes of protein should be given for every 100 Calories metabolized. Vitamins also should not be forgotten, especially with patients receiving a poor food intake. It is impossible at the present time to cover caloric requirements by the parenteral route. Glucose is always given along with water to cover obligatory water losses. Not only does glucose have an anti-ketogenic effect, and thus prevent acidosis, but also it exerts a protein-sparing effect. As was reemphasized by Gamble (1951), without glucose there is an augmented loss of protein in the fasting patient. Moreover, glucose in proper amounts will also reduce the solute load on the kidney (and thereby conserve water), and the loss of intracellular and extracellular water and of extracellular sodium. These reductions are of the order of 50% of that expected during starvation. For adults 100 grammes of glucose per day are required to produce this economy, and for the infant three grammes per kilogram are required. Adequate amounts of glucose will be ensured if a 5% solution of glucose is used to cover obligatory water losses.

Concomitant Replacement of Abnormal Loss.

After one has taken steps to correct dehydration and electrolyte loss, and has proceeded to administer maintenance requirements, it is necessary to cover losses from duodenal suction or fistulæ if these exist. Any type of gastro-intestinal suction obviously produces severe electrolyte deficits, and the importance of replacement cannot be over-emphasized. The administration of isotonic saline will not restore acid-base balance, for whether the losses come from the gastric juice or from the intestinal fluids, equal amounts of sodium ion and chloride ion will not be lost. (Incidentally, isotonic saline contains 150 milliequivalents of sodium and 150 milliequivalents of chloride per litre. Plasma contains 140 milliequivalents of sodium and 100 milliequivalents of chloride. Isotonic saline, therefore, contains excess chloride; hence, it can in no sense of the word ever be regarded as "normal"[1] and its effect is to favour acidosis.) Gastric juice contains greater amounts of chloride than of sodium. Metabolic alkalosis results from this loss. Intestinal juice contains more sodium than chloride. Hence, metabolic acidosis is the usual finding. Cooke and Crowley (1951) have simplified the approach to this problem by furnishing a gastric replacement solution and an intestinal replacement solution. The compositions of these replacement solutions are as shown in Table II. These solutions are isotonic, mimic the composition of gastric and intestinal fluid, can be given at rates up to 15

TABLE II.

Electrolytes Expressed in Milliequivalents per Litre.[1]

Solution.	Na.	K.	NH_4.	Cl.	Lactate.
Gastric replacement solution	63	17	70	150	—
Intestinal replacement solution ..	138	12	—	100	50

[1] Total cations, 150; total anions, 150.

cubic centimetres per kilogram per hour, have been well tried, and do not exert any deleterious effects when given by either the intravenous or the subcutaneous route. One should at least check the plasma bicarbonate level every other day while these solutions are being used. Every few hours the volume of gastric or intestinal suction is measured and an equal volume of the appropriate replacement solution is given, either by the same route as the maintenance fluid or through a separate intravenous infusion.

SECTION III: THE MANAGEMENT OF DISEASED STATES WITH RESPECT TO ELECTROLYTE AND WATER.

Deficit requirements are fulfilled by the administration of fluid and electrolyte measured in terms of kilograms of body weight. Unlike maintenance requirements, there is no relation to body metabolism.

In the discussion to follow it has been assumed that a 10% weight loss has occurred (10% dehydration), and the quantities of water and electrolyte mentioned should serve as a reasonable guide to therapy. High precision in parenteral fluid therapy is impossible and unnecessary; but no precision at all—no systemic approach—only serves to jeopardize the recovery of the patient.

In general, the extracellular deficits of body electrolyte and water in the child can be conveniently replaced—together with daily maintenance fluid—within twenty-four hours. In adults the replacement of electrolyte deficits takes longer. If abnormal losses continue, then varying amounts of deficit replacement must also continue. Here clinical judgement is essential. Although it is relatively easy to replace losses from the extracellular compartment, the restoration of cell composition is a process spread over days. Consideration for foods rich in potassium is well justified. Obviously one cannot include all conditions of fluid and electrolyte imbalance, and only a few major examples will be considered.

[1] The reason why isotonic saline was called "normal" was that in early days it was found that the freezing point of serum was the same as that of 0·9% saline.

Gastro-enteritis.

It has been shown by the work of Darrow (1946, 1952) that the deficits of the electrolytes sodium, potassium and chloride are almost equivalent in diarrhœa. The potassium losses are greatest. Acidosis arises partly because of the transfer of the sodium ion into the cells. The losses of extracellular electrolyte and water are crucial, in so far as they determine the degree of hæmoconcentration and the predisposition to shock. Water losses above 100 cubic centimetres per kilogram are frequent.

To assist restoration of extracellular relationships, an immediate infusion of 10 to 20 cubic centimetres per kilogram of Ringer-lactate solution is desirable. If shock is imminent, then resort to the transfusion of additional whole blood or plasma is important (20 cubic centimetres per kilogram). Once urine flow is confirmed, Ringer-lactate solution is exchanged for Darrow's solution ("K-lactate"), which contains sodium at a concentration of 120 milliequivalents per litre, potassium at 35 milliequivalents per litre, chloride at 103 milliequivalents per litre, and lactate at 53 milliequivalents per litre. Eighty cubic centimetres per kilogram of this solution, and 100 cubic centimetres per kilogram or more of 5% glucose and water should be administered. As the water deficit in a severe case will be greater than 100 cubic centimetres per kilogram, in such a case at least 250 cubic centimetres per kilogram of total fluid (deficit *plus* maintenance) are necessary within the first twenty-four hours. The maximum rate of potassium administration is 0·5 milliequivalent per kilogram per hour (14 cubic centimetres of Darrow's solution per kilogram per hour). If this régime is adhered to and kidney function is satisfactory, no danger will arise. There has been too much said about the dangers of potassium intoxication; this danger (bradycardia, muscle paralysis, heart block, cardio-vascular failure) mainly exists when potassium in high concentration is rapidly administered. If diarrhœa continues, deficit requirements must again be fulfilled and these requirements added to maintenance. Once the diarrhœa subsides, deficit requirements are reduced accordingly and oral feeding with equal parts of "K-lactate" (Darrow's solution) and 5% glucose solution can be begun, or the administration of food such as protein milk can also be started at 20 Calories per kilogram and increased to required levels. In mild cases the combination of equal parts of "K-lactate" and 5% glucose and water (200 cubic centimetres per kilogram per day) given by mouth is satisfactory. Maintenance requirements of electrolyte can be met with sodium chloride or Ringer's solution in appropriate amounts, as stated previously; but this should be necessary only for a very short period, as oral intake will improve. In severe cases, especially when latent infection exists, it may be necessary to continue to cover electrolyte deficits for several days, and here nutrition must be supported by plasma and by oral feeding of half-strength protein milk or some other feeding. In other words, the gain in withholding feeding can be exploited for only three or four days. At the same time it must be appreciated that protein storage and anabolism will not occur while there is alteration in tissue composition, such as cell potassium deficiency (Muntwyler, 1953).

The renal adjustments are such that with potassium loss there is a preferential and increased retention of sodium if sodium is supplied in large amounts. If the administration of sodium chloride as, for instance, 0·5% solution with glucose, is continued over periods of days without potassium, sodium retention will be such that obvious œdema will occur (Cheek, 1954*b*). Katcher reported œdema in 50% of his cases (Katcher *et alii*, 1953). Cardio-vascular collapse may supervene, and except for the œdematous tissues present at autopsy the pathologist will be at a loss to pinpoint the cause of death. Hence, it is my considered opinion that there is a greater potential danger with the use of sodium chloride only over long periods than with the use of solutions containing potassium and sodium. Furthermore, the efficacy with which potassium is utilized will depend on the coexisting sodium load, and for this reason "K-lactate" is the ideal solution for deficit replacement in gastro-enteritis. The syndrome of œdema, sodium retention and cardio-vascular collapse is sometimes seen in patients receiving ACTH without added potassium therapy. Under these circumstances the loss of cell potassium is so great that extracellular concentrations may also fail. Serum chloride and sodium concentrations are perhaps below normal, but the total amounts in the body are excessively high if there is no contemporary loss. With potassium depletion and available sodium and water there is loss of cell water and expansion of extracellular water.

Pyloric Obstruction.

In pyloric obstruction the pattern of electrolyte loss reveals a predominant chloride deficiency (Mateer *et alii*, 1951). The deficits of chloride, sodium and potassium are in the ratio of 3:2:1. In the worst cases (greater than 10% dehydration) these losses may amount to 30 milliequivalents of chloride, 20 milliequivalents of sodium and 10 milliequivalents of potassium per kilogram. Water loss will exceed 120 cubic centimetres per kilogram. Initially half isotonic strength saline with glucose to the extent of 20 cubic centimetres per kilogram should be given to restore extracellular volumes. Blood transfusion may also be necessary if incipient shock is present. Provided renal function is not impaired and urine flow has commenced, replacement of further deficits can be secured with a solution containing six grammes of sodium chloride per litre and three grammes of potassium chloride (isotonic in strength). One hundred cubic centimetres per kilogram should be used in a moderately severe case (10% dehydration). One can then proceed to fulfil maintenance requirements of water. If sodium chloride alone is used, the chloride concentration may fall even further. Alkalosis will remain or become worse. A hypotonic expansion of extracellular fluid will occur with retention of chloride, but this ion will be at a low concentration. Œdema of the tissues will present, which the surgeon will quickly recognize at operation. If this situation occurs, then potassium chloride alone must be given continuously as a 40 milliequivalent per litre solution. This will restore cell composition and probably cell water and reduce extracellular œdema, so that chloride concentration will rise to normal and acid base balance will be restored. Potassium, by restoring tissue composition, can alone perform these corrections.

Adrenal Insufficiency.

In adrenal insufficiency the deficits of sodium are a little greater than chloride, but for practical purposes the infusion of isotonic or hypertonic saline is satisfactory. Isotonic saline is sufficient if given in association with steroids. Again 80 to 100 cubic centimetres per kilogram or more of electrolyte solution will be required in most instances to reverse dehydration. Hypotonic solutions must be used with great caution. Blood transfusion is necessary in adrenal crisis. It is to be remembered that there is a relative increase in cell water, and extracellular fluid is dangerously diminished.

Salt Depletion.

Brief allusion has already been made to salt depletion. Patients with fibrocystic disease are known to be susceptible to heat stress (Di Sant' Agnese *et alii*, 1953). The concentration of sodium and chloride in sweat in these conditions approaches isotonicity. Water losses as sweat are not increased commensurately. Hence, these cases can be approached initially with a view to restoration of concentration deficits. Resort to hypertonic saline is frequently necessary. The same remarks apply to cases of pink disease in comparable circumstances, in which chloride losses in sweat and urine have precipitated a state of collapse. The infant's sweat electrolyte content under normal circumstances is rarely above 50 milliequivalents of sodium and chloride per litre (Cooke, Pratt and Darrow, 1950). Because the chloride and sodium losses in sweat are equivalent, alkalosis will predominate if there is a pathological loss of sweat electrolyte. Hence, in fibrocystic disease the relative overall loss of chloride from the extra-

cellular fluid leads to alkalosis and eventually to cell potassium deficiency. Additional amounts of chloride, sodium and potassium are necessary to restore cell composition. Again, these same remarks apply to pink disease, in which the chloride deficits appear to be twice as great as those for sodium or potassium (Cheek, 1954).

Tuberculous Meningitis.

In tuberculous meningitis the serum chloride and sodium concentrations are low; the serum potassium level may also be low and the pH and bicarbonate level are frequently high, indicating metabolic alkalosis and cell potassium loss. Investigations of these cases have revealed to me a hypotonic expansion of the extracellular fluid. Information gained from measurement of total water, and repeated observation of total chloride and body weight, suggest that there is a loss of cell water and cell mass (Cheek, 1954*a*; also unpublished data). Provided diarrhœa or vomiting is not conspicuous, it can be stated that the volume of distribution of bromide portrays the fact that total chloride content is normal or increased. There would seem to be no indication for giving excessive amounts of chloride. Indeed, elevation of concentration obtained by such procedures will be only transient. Here the low serum chloride concentration demonstrates the fact that there is a generalized lowering of osmolarity throughout the body, and if one did wish to correct extracellular concentrations this might be achieved only by the primary restoration of the principal cell electrolyte—namely, potassium. Added electrolyte and water should, therefore, be given only when the circumstances of dehydration result. Evidence also suggests that dehydration in these cases is mainly at the expense of cell water (Cheek, 1954*a*). It must further be appreciated that in tuberculous meningitis there is a loss of homœostatic controls. Such patients can neither conserve chloride, nor effectively excrete a chloride load (Rapaport, West, Brodsky, 1951). Investigation of one single patient revealed that he was capable of a satisfactory water diuresis.

Diabetic Coma and Acidosis.

Relatively small deficits of potassium can exist in the body without undue deleterious effect. Indeed, as Bennett (1953) has shown, patients receiving continued adrenal hormone therapy all have some deficit of this electrolyte. To some extent the replacement of potassium by sodium in the body cells with alkalosis does not seem to interfere with well-being unless these changes become extensive. If this happens, then œdema, cardiac failure and actual degeneration of kidney tubule cells may result. We could restate this situation by saying that mild cell acidosis is compatible with health. However, if a significant sodium deficiency is superimposed on potassium and chloride deficiency, extracellular acidosis will develop and a serious situation will arise (Fourman and Ainly Walker, 1952). So gross is the dysfunction of cell metabolism that cardiovascular collapse may easily supervene. In diabetic acidosis and diabetic coma one is aware that large losses of intracellular and extracellular electrolyte have occurred through persistent vomiting and osmotic diuresis. The latter is most significant and is due to high blood sugar levels (Brodsky *et alii*, 1949). It is a simple experiment to deplete an individual of electrolyte by injecting into the veins quantities of osmotically active solutes such as glucose or mannitol. The losses of water in diabetic coma are also great (generally exceeding 80 cubic centimetres per kilogram), but the water losses are not so great as those of electrolyte. Dehydration exists together with a generalized hypo-osmolarity. Because the ratio of sodium loss to chloride loss is of the order of 1·3 to 1·0 (Nabarro, 1952), acidosis predominates. Acidosis is also dependent on the fact that ketone bodies are circulating in the body fluids. The pH reading may then be at its lowest limit compatible with life. The extracellular fluid is reduced in volume, but in this situation volume is preferentially preserved and concentration is sacrificed. With the loss of cell electrolyte (potassium, phosphate and magnesium) there is also a loss of cell water (Knowles and Guest, 1953), and this reserve of cell water is probably drawn on until the last, when peripheral vascular collapse and rapid contraction of blood volume result.

This state of affairs represents a medical emergency that must be dealt with by a team of workers directed by the senior physician. This is no circumstance in which therapy can be left in the hands of the resident staff. The mortality from the condition should be almost nil. It is presumed that insulin is given in adequate amounts, for we intend to mention only those aspects which pertain to water and electrolyte. These necessities must be rapidly restored within the first three hours. Some clinics begin with two intravenous infusions at the one time.

Restoration of extracellular fluids is the first essential. This can be achieved by the use of Ringer-lactate solution (40 to 50 cubic centimetres per kilogram), which contains chloride and sodium in physiological proportions. Extracellular acidosis can be partly relieved by the infusion of 20 cubic centimetres per kilogram of one-sixth molar lactate solution through another intravenous infusion site. After this, blood or plasma (20 cubic centimetres per kilogram) can be given through the same site, then this infusion can be removed. For a 20 kilogram child 800 to 1000 cubic centimetres of Ringer-lactate solution should be given before the end of two and a half hours, together with 400 cubic centimetres of plasma and 400 cubic centimetres of one-sixth molar lactate solution. At the end of this period urinary function should have improved and the non-protein nitrogen value is likely to have fallen and may even be within normal limits. The administration of potassium lactate solution (Darrow's solution) containing 36 milliequivalents of potassium per litre can then be started, and 50 cubic centimetres per kilogram may be administered. At the end of this infusion, the giving of maintenance requirements should be commenced and completed within the twenty-four hours period. It is assumed that the diabetic condition is brought under control with insulin. Glucose (5%) in water should not be used while the blood sugar level exceeds 500 milligrammes per 100 cubic centimetres, for one is endeavouring, among other things, to obliterate the osmotic diuresis. Some may prefer to start the potassium lactate infusion by clysis during the second hour. Although potassium and phosphate concentrations are high initially owing to hæmoconcentration, the levels fall very rapidly with rehydration and restoration of glucose metabolism. Death has been reported from dangerously low potassium levels. In any event, if the serum potassium level falls below 3·0 milliequivalents per litre, potassium replacement should be started. When consciousness is regained, potassium-containing fluids (such as orange juice) must be given. Several days will expire before losses of cell potassium are restored, and the electrocardiogram if followed in series will frequently demonstrate a prolonged *P-R* interval and depression of the *S-T* segment for several days. During the subsequent convalescence foods rich in potassium must be offered. Some investigators recommend the use of phosphate, magnesium and calcium, in addition to potassium, for cell repair (Nabarro, 1952). There is added logic in this approach; but no better results have as yet been demonstrated. However, work at present in progress indicates that solutions containing potassium chloride at isotonic strength alone seem efficacious in combating successfully the cellular loss (Knowles, personal communication). Nor-adrenaline also proves of great value in combating peripheral vascular collapse.

The Post-Operative Patient.

Serious operations with much trauma are associated with a concomitant stimulation of the pituitary-adrenal axis. Negative nitrogen and potassium balance with sodium retention is a concurrent phenomenon. Provided excessive vomiting or contemporary losses are not occurring, maintenance fluid and electrolyte only should be given post-operatively. Some prefer to reduce the sodium and chloride requirement by 50%. On the third day one should watch for potassium deficiency. Fluids given by mouth (if possible) will reduce potassium losses. In this direction

meat broths and fruit juices are most helpful. If potassium levels fall significantly, replacement must be undertaken.

If one is dealing with gastric losses or post-operative jejunostomy with drainage, then, as has already been pointed out, fluid lost must be replaced and electrolyte given according to the magnitude of the measured losses. Here the use of intestinal and gastric replacement solutions simplifies a difficult problem (*vide* Section II).

Anuria and Oliguria and Lower Nephron Nephrosis.

Renal damage and ischæmuric episodes which occur in the renal tubules resulting from the effects of toxins give rise to a failure of renal function. It is important under these circumstances to maintain proper hydration by giving the maintenance requirements of water and electrolyte for sweat, stool and insensible water only. In this way blood volume will be maintained. If abnormal losses have occurred through vomiting, then approximate quantities of electrolyte calculated to restore this loss must be injected. The protein-sparing effect of glucose must be remembered. One-quarter of the caloric requirement is given as glucose. No potassium is given unless there is definite deficiency of this ion. Hence, 60 cubic centimetres of glucose (5%) and water per 100 Calories metabolized can be given. For a child weighing 20 kilograms this would amount to some 700 cubic centimetres of fluid per day containing glucose and minimal amounts of sodium and chloride. When diuresis appears, the urine is generally isotonic or resembles an ultrafiltrate of plasma, and large losses of electrolyte can be rapidly incurred. Urine should be collected and the contents estimated. Isotonic infusions will restore these losses.

Salicylism.

Lastly we shall consider overdosage of salicylates, which is a relatively common problem. Salicylates lower the prothrombin level of the blood and sometimes give rise to bleeding; they stimulate the respiratory centre and interfere with liver function, causing glycogen depletion and ketosis. Two grammes per kilogram per day will produce these effects. Abnormal stimulation to the respiratory centre gives rise to overbreathing and respiratory alkalosis. The carbon dioxide tension in the lungs decreases and likewise the serum bicarbonate, but the latter falls to a lesser extent. The pH is, therefore, alkaline. Responsibility is relegated to the kidney to make adjustments for these changes. Chloride is retained and the excretion of sodium and potassium is augmented. When the stimulus to the respiratory centre subsides, the greater overall loss of sodium relative to chloride and water losses with impaired renal function leads to metabolic acidosis, and the pH falls below 7·35. Water losses are high during hyperventilation. The original animal experiments of Eichelberger and Hashings (1937), and the more recent human experiments of the Australian investigators (McDonald, Coats and Munro, 1953), suggest that there is a shift of water into body cells during hyperventilation. The latter workers noted a loss of one litre of water during hyperventilation over a four-hour period. The studies of Rapaport *et alii* (1946), which have been extensive on the subject, indicate an alteration of calcium metabolism in the hyperventilation syndrome. There is no consensus of opinion as to the correct approach to salicylism, but it has been shown that alkalinization of the urine enhances the excretion of salicylates. We know also that sodium losses are greater than chloride, and that glycogen is depleted in the liver. It is recommended that 100 cubic centimetres per kilogram of half-strength Ringer-lactate solution be given and then maintenance requirements supplied.

Conclusion.

We began by paying homage to the kidney, and, indeed, one of the principal aims in fluid therapy is to facilitate and restore renal function. However, it can by no means be assumed that there is adequate renal function in all circumstances of extrarenal disease with dehydration and electrolyte loss. It is likely that many of the changes occurring in muscle cell composition may also be taking place in the specialized cells of the renal tubule. The replacement of electrolyte and water in approximately the correct proportions has thus been emphasized.

It can be predicted that the future will emphasize further the understanding of cell electrolyte change. For example, attention to the role of magnesium will be intensified. We know, for example, that young animals are more easily rendered deficient in magnesium than are mature animals. There is not a substantial reserve of available magnesium in the body. Muscle tremors, spasm, hyperexcitability, confusion, disorientation, convulsions and cardio-vascular dysfunction appear early in young animals when this electrolyte is lacking. Like potassium, it is not rapidly replaced; the serum concentration is a poor index of body status, protein synthesis does not occur in the face of cell magnesium loss, and deficiency can be produced by prolonged parenteral fluid therapy. Calves develop neonatal tetany due to magnesium deficiency if fed on cow's milk only. Myocardial fibrosis, neurological degenerations and nephrotic changes in the kidney tubule can be demonstrated pathologically in the absence of this electrolyte. It is known that magnesium plays a vital role in the activation of the enzyme adenosine triphosphate, and that a high calcium, potassium, ammonium chloride or protein intake tends to aggravate magnesium loss. Of particular interest is the finding of generalized renal calcinosis in magnesium deficiency. The occurrence of clinical magnesium deprivation has recently been reviewed by Flink *et alii* (1954). Losses can be detected in cases of *delirium tremens*, in post-operative states, in diabetic acidosis, and under circumstances of malnutrition.

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ASPECTS OF TREATMENT OF TUBERCULOSIS.

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THE following résumé of the more important trends in the treatment of tuberculosis is based upon observations made in Britain, America and Canada during 1952 and 1953.

The most important problems in the treatment of pulmonary tuberculosis concern the duration and type of chemotherapy, the present place of bed rest and reversible collapse procedures, and the place of resection for non-cavitated lesions.

Brief mention has been made of some aspects of the treatment of extrapulmonary tuberculosis and of the rehabilitation of the tuberculous patient.

Chemotherapy.

There are still some differences of opinion about whether chemotherapy should be short-term or prolonged in application. The concept that chemotherapy was of value only as short-duration therapy originated when streptomycin was first employed and found to have a short-lived effectiveness owing to the development of bacterial resistance. However, the combination of PAS with streptomycin usually delays the development of serious drug resistance for many months. This, together with the availability of isoniazid, led to the acceptance of prolonged chemotherapy in the

United States of America and Canada and to a lesser degree in England.

Long-term chemotherapy with streptomycin and PAS has been used at the Veterans Administration Hospital, Sunmount, New York, since the end of 1948. It was accepted as a beneficial therapeutic procedure after many patients with far advanced disease appeared to derive benefit from continuous chemotherapy lasting beyond four months. In contrast to short-term chemotherapy, many more of these patients became "sputum-negative" and in a relatively high percentage the cavities closed. It was found that spread of the disease was rare within at least the first twelve months of treatment, and improvement was generally maintained during chemotherapy provided this was uninterrupted. However, if chemotherapy was stopped and the number of bacilli in the sputum increased, repeat treatment was less likely to control the disease—an observation emphasizing the superiority of continuous chemotherapy to interrupted courses.

The Results from Prolonged Chemotherapy.

During three months at Sunmount I was able to observe that the results of long-term chemotherapy were strikingly good. The follow-up results of the first 101 patients treated were being analysed, and I had the privilege of going through some of the records. A majority of the patients had far advanced disease, and yet 61 reached what was called the target point; that is, all their cavities closed and they became consistently "sputum negative" and stable radiologically. Of these successful cases, in 34 the patients were then submitted to resection of the residual diseased areas, and in the remaining cases resection was not performed owing to contraindications. Most of the patients had been followed for between two and three years after the cessation of chemotherapy, and in this time only two of the 61 reaching the target point had relapsed; one of these had been submitted to resection and one not. In view of the advanced type of disease treated, the results are especially satisfactory. In the 40 patients not reaching the target point, only nine had inactive disease at the time of follow-up examination, and 14 had died of tuberculosis. There was, therefore, a considerable difference in prognosis, which depended upon whether the target point was reached or not.

The results obtained at Trudeau Sanatorium were somewhat similar. Roger Mitchell *et alii* (1953) found that of 245 patients, 85% had sputum free from tubercle bacilli after six months' continuous chemotherapy, and that the failures were mainly attributable to previous or irregular chemotherapy. At Weston Sanatorium, Toronto, the results analysed by Alec Capon were similar to those obtained in the other two institutions.

The type of patient admitted to each sanatorium mentioned differed to some degree, so the fact that the three were unanimous in reporting favourably upon long-term chemotherapy is strong evidence for its therapeutic effectiveness. It is now well established that chemotherapy prolonged for over six months will lead to a higher percentage of sputum conversion and of cavity closure than chemotherapy of short duration.

Types of Chemotherapy.

There are no really satisfactory controlled studies of different drug regimens used for more than four to six months. Excellent studies have been carried out on short-term chemotherapy. However, there is some doubt whether the results of these studies are applicable in prolonged usage. The most effective regimen is probably that of streptomycin, PAS and isoniazid together, and this is used by some hospitals as a routine measure—for example, Weston Sanatorium, Toronto. However, the superiority of the three drugs over two-drug combinations is not overwhelming, so that until further information is obtained, the three-drug combination can be reserved for seriously ill patients.

There is as yet no clear-cut guide as to which of three possible two-drug combinations is the best, and they appear to be almost equally effective. The streptomycin and isonicotinic acid hydrazide (INAH) combination has the disadvantage that there is the risk of resistance to the two best drugs without a clear-cut therapeutic advantage being obtained over the use of PAS with either streptomycin or INAH. The Medical Research Council of the Privy Council in England warned that twice-weekly administration of streptomycin may not prevent resistance to INAH as effectively as does the daily administration of streptomycin. For this reason in England, when streptomycin was used with isoniazid it was usually given daily.

There are three well-tried combinations of streptomycin and PAS: (i) streptomycin, one gramme daily, with sodium PAS, 16 to 20 grammes daily; (ii) streptomycin, 0·5 gramme daily, with sodium PAS, 16 to 20 grammes daily; (iii) streptomycin, one gramme twice weekly, with sodium PAS, 16 to 20 grammes daily. These three regimens are approximately equally effective in short-term trials. However, it was thought at Sunmount that for prolonged chemotherapy streptomycin, one gramme daily with PAS, was a little more effective than streptomycin, twice a week, and PAS. With the latter regimen resistance to PAS is probably more frequent than with the daily administration of streptomycin. In the bacteriological study of resected lesions, it was shown that tubercle bacilli were more difficult to cultivate from closed lesions after the daily administration of streptomycin and PAS than after streptomycin, twice a week, and PAS. In spite of these theoretical disadvantages, streptomycin is widely used twice a week and appears to be effective in the majority of cases.

The third two-drug combination, INAH and PAS, has received the least attention, but has the definite advantage that both drugs are administered orally.

An interesting finding in both United States and Britain is that some organisms that become resistant to isoniazid are more or less avirulent for guinea-pigs and mice, although growing readily on culture. This produced the hope that such organisms would also have a diminished virulence for the human host. It was the view of some in America that spread was uncommon in patients whose bacilli became resistant to isoniazid. However, Steenken at Trudeau Sanatorium found that spread has occurred in patients with bacilli resistant to INAH, although the bacilli were avirulent for guinea-pigs. This shows that avirulence in guinea-pigs does not necessarily mean avirulence for humans. Further investigation is awaited.

Toxicity.

Toxicity and hypersensitivity are probably least common with streptomycin and INAH, and most frequent with streptomycin and PAS. Such complications can be handled in three ways: (i) by substitution of another drug; (ii) by desensitization; (iii) by the use of ACTH and continuing chemotherapy. ACTH with chemotherapy has been safely administered in England by Houghton.

Other Drugs.

If there is pronounced resistance to two of the major agents, then long-term chemotherapy is contraindicated. In such cases the use of chemotherapy to "cover" surgery is often required. For such cases or in the presence of resistance to all three major drugs, viomycin can be used, two grammes every third day. If there is still sensitivity to PAS, it is preferably used with viomycin. The main value of viomycin is to "cover" resection in patients with bacilli resistant to streptomycin and INAH.

"Terramycin", one to two grammes daily, can be used in combination with streptomycin, as it delays the development of resistance to streptomycin. It is of most value when there is resistance to PAS.

Isopropylnicotinic acid hydrazid has been found too toxic for general use.

Type of Case Suitable for Long-Term Chemotherapy.

Chemotherapy is frequently used in all cases of recent or active tuberculosis irrespective of extent and dynamic status. In minimal disease chemotherapy will prevent spread and hasten resolution. For disease that regresses spontaneously, it is probable that chemotherapy will hasten regression further. There is some evidence that prolonged

chemotherapy may prevent or delay subsequent relapse, and for this reason it is being tried for tuberculous pleural effusion in the absence of obvious pulmonary infiltration.

Progress of Patients during Chemotherapy.

Patients treated with prolonged chemotherapy can be divided into two main groups according to whether or not they reach what is known as the target point and show the following features: (i) sputum and gastric contents free from tubercle bacilli for three consecutive months; (ii) closure of all cavities; (iii) X-ray stability (except for slow shrinkage of lesions). Patients who reach this therapeutic target have a relatively favourable outlook, whereas those that fail to do so can be considered chemotherapeutic failures and will usually do poorly unless they have some form of collapse or surgical treatment in addition to chemotherapy. In general the most pronounced improvement with prolonged chemotherapy is obtained in the first six months, and the majority of patients reaching the target point do so in six to nine months.

Management of Patients Who Reach Target Point.

There is considerable doubt as to the best management of patients reaching the target point. In 1950 at Sunmount, it was considered advisable to resect residual necrotic lesions after the attainment of the target point. When possible the residual lesions were removed by wedge resection, only a small amount of lung tissue being removed. This has proved to be a relatively safe procedure during prolonged chemotherapy, and although the surgical risk is not entirely negligible, such tuberculous complications as broncho-pleural fistula and empyema are seldom if ever encountered. This surgical approach was based upon the findings of Medlar that many residual lesions still maintained a small bronchial connexion and appeared to be potential sources of spread of the disease. Also earlier clinical studies had shown that prior to the use of long-term chemotherapy about 30% of patients with closed lesions eventually relapsed.

The work done since 1950 has raised considerable doubts as to the validity of the concepts advanced then. First, the bacteriological findings, now confirmed in many laboratories, did not support the pathological evidence that the residual closed lesions were a source of danger. Even when tubercle bacilli were readily seen by direct examination of the lesions, in only a small percentage of cases was it possible to grow them on culture or infect animals with them. Although it would be unsafe to conclude that the bacteria are not viable under any circumstances, it is evident that if they are not dead, their viability is considerably impaired. The recovery of viable bacilli was inversely related to the duration of chemotherapy.

As non-viable bacilli have been reported in closed lesions from patients not treated by chemotherapy, it is considered that chemotherapy assists in bringing about, but is not the sole cause of, the phenomenon.

A second finding has been that in a small percentage of cases the residual lesions have been insignificant at exploratory thoracotomy. Contrary to expectations, what were presumably once necrotic lesions have disappeared during prolonged chemotherapy, without operation. It raises the possibility that this may occur more frequently if given time.

Thirdly, the doubts raised by these observations have been increased by follow-up studies of patients who were considered unsuitable for operation owing to poor respiratory function or for other reasons. As has already been mentioned, these patients, provided that they attained the target point, have done very well, especially when one considers their advanced state at the start of chemotherapy. The relapse rate in the first year is much lower than that anticipated from experience with short-term chemotherapy, and is of the same small order as in the cases in which operation is undertaken.

It is clear that no dogmatic statement can be made regarding the place of surgery in the treatment of closed lesions after prolonged chemotherapy. There is an urgent need for this problem to be seriously investigated by a trial with controls. At the present time there is a definite lack of knowledge, and such criteria as size of the lesion or previous relapse may be important, but there is a lack of convincing evidence on the question. Even before the use of prolonged chemotherapy, there was considerable doubt as to the wisdom of resecting closed lesions. For example, if we consider the so-called tuberculoma, which surgeons throughout the world frequently excise, the available evidence suggests that patients with such lesions do well with conservative management. Moyes (1951) followed a series of patients with tuberculoma of the lung for from three to fifteen years, and found that of 34 patients treated conservatively, 91% were alive and well at the end of surveillance, and none had died. Despite good prognosis, in 50% instability of the lesions was shown at some time.

It is clear that with or without resection, it is likely that the prognosis is considerably improved by prolonged chemotherapy. There are still some advocates of thoracoplasty and plombage for certain types of closed lesions, but the case for such procedure is uncertain.

Duration of Chemotherapy.

The duration of chemotherapy has been determined partly by the progress made by the patient, and partly arbitrarily. It has been common practice to continue chemotherapy for about six months after the therapeutic target point has been reached. The total duration of chemotherapy is therefore related to the time taken to reach the target point. Whether the continuation of chemotherapy for six months after this point has been reached is too short or long a period is really unknown.

Patients Failing to Reach Target Point.

A most important point is, how long should chemotherapy be continued in the hope that the target point will be reached? For both sputum conversion and cavity closure, the majority of satisfactory results will be obtained in nine months. Further, it has been found that patients who still have large cavities after six months will usually develop bacterial resistance with the two-drug regimen. It is convenient, then, to consider six months as an important assessing point, when operation is seriously considered for all those who have not reached the target point. Various factors help in making a decision. The size of any cavity is important. Those that are still large or moderate in size are unlikely to close with further chemotherapy, but one small and decreasing in size may still close, and it is then reasonable to defer a final decision for a further three months. Good quality tomograms, anterior, posterior and lateral, are necessary, and when there is some doubt, it is probably good practice to manage the patient as having a cavity.

Bacteriological investigation may be of considerable assistance. For example, if examination of the sputum continues to give strongly positive results after five or six months, resistance is likely to develop, and deterioration follow. It has been found both at Papworth in England and in the Veterans Administration in America that quantitative bacteriological investigation is of considerable help clinically. For example, if a patient starts with a positive culture which produces a confluent growth on the medium, and during five months has had a decreasing number of colonies cultivated until the last report indicated only four colonies, then, even though positive, this is a favourable report, as it is likely that the future attempts at culture will give negative results. On the other hand, serial cultures showing increasing colony counts are a bad sign, and are usually associated with bacterial resistance.

It is the practice in some laboratories to carry out sensitivity tests on all positive cultures from patients receiving chemotherapy. From the clinical aspect it is fairly clear that the sensitivity tests are of most value when they are performed on solid media, so that it is possible to have a quantitative estimate of the number of bacilli sensitive and resistant at any specified concentration.

Chemotherapy can be continued with benefit long after small numbers of resistant bacilli appear, and deterioration does not usually occur until the vast majority of bacilli are resistant. Serial sensitivity tests indicate when complete resistance is being approached; and provide an added indication for operation.

For patients failing to reach the target point in six to nine months, and for whom surgery is contraindicated, it is advisable to continue chemotherapy until improvement ceases, as in some the target point is finally reached, and in others the sputum becomes free from tubercle bacilli and cavities are converted into a smooth-walled cyst-like space.

Although six months is a favourable time for assessing most patients, there are probably some in whom failure to reach the target point can be anticipated and operation considered earlier. Patients unwilling or unable to complete prolonged chemotherapy come into this category. Similarly, patients who already show some bacterial resistance at the commencement of chemotherapy are more likely to be failures, as are those with a large cavity at the apex. Even for those patients who are likely to fail to reach the target point, it is usually advisable to wait four to six months if possible, as by then a good deal of improvement has occurred, the disease is less active, the sputum is often free from tubercle bacilli, and surgical complications are probably fewer.

The Place of Bed Rest and Reversible Collapse Procedures during Chemotherapy.

There has been a long controversy concerning the value of bed rest in the treatment of tuberculosis. Short-term chemotherapy made little impact on the established bed rest policy, and it was generally accepted that bed rest and chemotherapy were synergistic. Actually it has yet to be shown that bed rest adds to the effectiveness of prolonged chemotherapy. D'Esopo at Sunmount was a convinced advocate of bed rest until he noticed that of the patients receiving chemotherapy, the inevitable undisciplined ones did as well as those remaining on bed rest. It became the practice at Sunmount to allow most patients up for about four to six hours daily once their sputum ceased to contain tubercle bacilli. There were no obvious ill effects, and D'Esopo became a strong advocate of the need for reexamining the place of bed rest therapy during chemotherapy.

However, as has already been pointed out, in any series treated there is a proportion of patients failing to reach the target point, and to keep this proportion to a minimum, it is to be expected that bed rest and even postural treatment will still have a place in therapy. My own impression was that, especially for patients with no cavities or small cavities, strict bed rest was no longer essential, but that bed rest and postural treatment probably still had a place in closing larger cavities.

Similar remarks apply to the reversible collapse procedures, artificial pneumothorax and pneumoperitoneum. Unlike bed rest, there is a considerable tendency to cease to use these procedures. Although there are many centres still using pneumothorax, in others it is practically never used. This is because of its complications—empyema, thickened pleura, and non-expandable lung leading to severe function loss. Its value in controlling the disease, if it achieves cavity closure, has not been seriously disputed, and has been fairly convincingly demonstrated by Foster Carter and others at Frimley Sanatorium. There are those in the United States of America who think they may have swung to an extreme, and that there may still be a place, although a small one, for the use of pneumothorax. A possible place for pneumothorax would be as short-term therapy to close cavities during chemotherapy.

Pneumoperitoneum is usually performed without a phrenic crush, as this leads to a loss of respiratory function which is sometimes permanent. Pneumoperitoneum is believed by some—for example, Roger Mitchell, of Trudeau—to play an important role in cavity closure during the course of chemotherapy. The subject still requires further investigation, but the existing information suggests that the procedure still has a place, and that it is safer than pneumothorax.

Surgery.

In the original cases treated at Sunmount it was shown that the prognosis was poor for those patients who failed to reach the target point, and it was considered that operation was essential for such patients if it could be undertaken. There are some advocates of a widespread use of resection for these patients, but owing to such complications as broncho-pleural fistula, there are many who favour thoracoplasty if this is likely to be successful, and reserve resection for those conditions in which it is thought that thoracoplasty is likely to fail—for example, giant cavities, cavities in solid lesions, the presence of bronchostenosis, and sometimes the presence of bronchiectasis. At Sunmount, resection was preferred only if the sputum had become negative. Results of resection were good with this plan, and tuberculous complications were infrequent. At Weston Sanatorium, Toronto, of 30 patients with cavitation, only five still gave a positive cultural result after six months' chemotherapy. Thus, in practice, the Sunmount precaution would prevent resection in only a small percentage of the cases in which long-term chemotherapy is employed.

In all countries there is a trend to conserve lung tissue when a resection is performed. The extent of resection is judged finally by palpation at operation. It is believed safe to leave lung tissue which has had disease in it, but is without appreciable disease at operation, and in some cases the major diseased area is removed and palpable diseased tissue is left behind. To estimate the extent of the palpable diseased tissue prior to operation and to help decide between collapse and resection, both tomography, and to an increasing extent bronchography, are used. Thoracoplasty following resection is still performed by many after lobectomy; but although most surgeons with pre-chemotherapy experience are convinced that over-expansion of non-resected lung may lead to exacerbation of latent disease, the experience has been that this is unlikely to occur with prolonged chemotherapy. However, this potential risk is an added reason for removing as little lung tissue as possible.

Plombage thoracoplasty is advocated by some surgeons. In England plastic sponges are being used instead of spheres, and have the advantage of being able to be sterilized by boiling. The loss of function following this operation is believed to be less than after standard thoracoplasty or lobectomy, and it would appear to have a definite place in the treatment of the "poor risk" patient with upper zone disease.

Pulmonary Function.

There was a growing reliance upon respiratory function tests prior to operation, especially in the "border-line" case.

Various Other Aspects.

Primary Tuberculosis in Children.

Dr. Lincoln at Bellevue Hospital has until recently not used chemotherapy for symptomless children with primary tuberculosis. Chemotherapy has been administered for complications, and the mortality rate was reduced from 23·6% to 2·9% by this procedure. Dr. Lincoln now considers it warranted to carry out a controlled trial of the value of a prolonged course of chemotherapy in preventing the development of complications. This trial, in which isoniazid and PAS were used, was in progress during my visit to Bellevue, but no results were available.

At Sully Hospital in Wales, interesting work was being done upon the surgery of enlarged mediastinal glands. These not uncommonly cause stridor, atelectasis and obstructive emphysema, or may rupture into a bronchus.

It has been the practice at Sully to remove or evacuate caseous glands which are producing, or are likely to produce, complications. It has been found to be a relatively safe procedure. However, the bronchial damage was not always reversed. The work would indicate that the procedure is fully justified when enlarged glands are producing cyanosis and are a threat to the patient's life. It may have a wider application, although it has yet to be established that in general the procedure produces better results than non-surgical treatment.

Tuberculous Lymphadenitis.

At Sunmount, and at Weston Sanatorium, patients with tuberculous lymph nodes had been treated successfully with long-term chemotherapy.

Tuberculous Pleural Effusion.

As the tuberculous relapse rate is at least 25% in patients with pleural effusion followed for five or more years, the use of chemotherapy in preventing this development is being explored.

In America, the Veterans Administration have been trying the use of a routine four months' course of chemotherapy for all patients with pleural effusion. Dr. D'Esopo advocates the trial of a year's course. There is evidence that if the larger effusions are aspirated within the first month, delayed absorption and gross pleural thickening are largely avoided (Campbell and Moon, 1954).

Miliary and Tuberculous Meningitis.

The use of isoniazid in combination with PAS and streptomycin in miliary and tuberculous meningitis was being tried in most centres with encouraging results. Some investigators were omitting the intrathecal administration of streptomycin, but there were many who were not yet convinced that this could be done safely.

Orthopædic Tuberculosis.

The most interesting orthopædic work that I saw was at Weston Sanatorium, and the following is part of a report compiled by H. S. Coulthard (1953), who has had wide pre-chemotherapy experience of orthopædic tuberculosis.

> Long-term therapy (12-18 months) with streptomycin, Gram 1, semi-weekly and PAS daily, along with demobilization has proved to be much more efficacious than any previous regimen, with the exception of daily streptomycin and PAS for six months, and is now used exclusively for these cases. Isoniazid therapy was added in October, 1952.
>
> (1) In early cases without much or any joint destruction the results have ranged from partial to complete recovery of normal function, without relapse on weight bearing (longest follow-up 15 months exercise).
>
> (2) In cases where joint cartilage or intervertebral disk was completely destroyed, early bone ankylosis (i.e. in one year or less) was observed under streptomycin therapy, and no surgical operation was required.
>
> (3) In the remaining cases where it was evident that early ankylosis could not be obtained because of intervening cartilage or disk, bone grafting or arthrodesis was done, as formerly, but at an earlier date, so that the period of hospitalization was shortened.
>
> (4) In patients with multiple lesions, the use of streptomycin brought about simultaneous healing of all lesions, so that a series of operations was avoided and time was saved even though the overall period of hospitalization was of necessity longer than in cases with a single lesion.

Genito-Urinary Tuberculosis.

Most of the recent work on chemotherapy of genito-urinary tuberculosis has dealt with short courses of chemotherapy. Dr. Latimer, of the Bronx Veterans Administration Hospital, had found this to be curative in renal tuberculosis only when pyelography reveals little or no abnormality. When there is more extensive abnormality he advises surgery and prefers partial resection of the kidney when this is possible. He favours, as do most others, the removal of infected epididymi. However, at Weston Sanatorium they have found that the removal of an epididymus does not prevent later spread to the other side, and with chemotherapy they consider that surgery is even less necessary.

Other Work.

In Britain certain investigations are being made on factors that favourably alter the organism's reaction to the tubercle bacillus. If such an approach was to prove successful, it could be even more valuable than the anti-bacterial approach.

D'Arcy Hart and others have demonstrated the in-vivo effectiveness of detergents in treating tuberculous animals. These substances have no direct action upon the tubercle bacilli.

Honor Smith and others have used tuberculin with chemotherapy, and Houghton has used ACTH with chemotherapy. This latter treatment is of value if hypersensitivity develops to one of the drugs. It has been found to have no deleterious effect on the patient with tuberculosis, and may have a favourable influence.

Rehabilitation of the Tuberculous Patient.

The placing of ex-patients back in suitable employment is a problem in most countries, especially those patients previously employed in some form of heavy manual labour, and others previously employed in lighter but unsuitable work. After studying the various schemes, such as those at Papworth and in the Veterans Administration, and the Canadian sanatoria, I felt that each scheme had valuable aspects. The Canadian approach was of the widest value; the emphasis was on improving the technical ability of a patient so that, when he was fit to return to work, he had either acquired a new skill or improved on his previous skill. The plan at Toronto and Hamilton started early in the patient's treatment, and the large staff of teachers attached to the sanatoria provided a wide range of study. For some patients this might be purely cultural or diversional, and many of the older patients learnt a foreign language. Younger patients had the opportunity of vocational training. For those wishing to complete their schooling, lessons were provided and assistance was also given to those who were preparing to take technical and university courses. Business and clerical courses were also conducted.

An extension of this type of scheme, but on a smaller scale, was conducted at Pinewood Hospital, England, where there was a rehabilitation unit for university students. Students throughout Britain could spend their convalescence there, and carry out organized study with the help of visiting tutors and lecturers. This scheme worked well, although applying to only a small number of patients.

The provision of facilities in the sanatorium for academic and technical training seems to be a definite advance. Post-sanatorium facilities for technical and practical training in such workshops as at Papworth are also a great advantage for patients requiring retraining.

The Care of the Mentally Ill with Tuberculosis.

There is a move towards special units for the treatment of tuberculosis in the mental hospitals. There are a number of such units in the Veterans Administration in the United States of America and also in England. In Canada, the Woodstock Hospital provides for the treatment of all the mentally ill patients with tuberculosis from the Province of Ontario. The physicians at Woodstock are also responsible for an energetic case-finding programme in the mental hospitals of the Province.

Both the mental illness and the tuberculosis were treated concurrently. The mental illness seldom contraindicated the usual treatment of tuberculosis, and it has been found quite safe to use shock treatment in the treatment of the mental illness.

It is probable that a unit for the treatment of mentally ill tuberculous patients would be of considerable advantage in the more populous Australian States.

Conclusion and Summary.

There has been an increasing acceptance of prolonged chemotherapy in the treatment of tuberculosis. This is leading to a reevaluation of previous practice, and has already affected the use of temporary collapse procedures, threatens to some extent the use of bed rest, and is throwing doubt on the need for operation for non-cavitated pulmonary lesions.

Although antibacterial therapy has proved of tremendous importance, it has certain limitations. Research proceeding on the means of enhancing the organism's reactions against tuberculosis may eventually provide valuable results.

Rehabilitation and the treatment of tuberculosis in the mentally ill have been discussed.

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THE SINGLE DAILY DOSE OF SODIUM PARA-AMINOSALICYLIC ACID USED IN CONJUNCTION WITH STREPTOMYCIN IN TUBERCULOSIS.

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IN July, 1952, at the Mountain Sanatorium, Hamilton, Ontario, it was decided to give one single daily oral dose of 12 grammes of sodium PAS to 30 adult patients with pulmonary tuberculosis to determine whether this régime would lessen toxic side effects of the drugs. It was found during the following two months that the patients preferred taking the single dose. No toxic side effects were found, and in September, 1952, the whole patient population of the sanatorium taking streptomycin was transferred to the one daily dose. This population included patients with all forms of tuberculosis, both medical and surgical. Children were put on one daily dose, but the dosage was adjusted according to weight.

A study was then undertaken to determine what was the effect of this single daily dose of sodium PAS on the emergence of streptomycin-resistant strains of tubercle bacilli, and whether the preliminary observation of lessened toxic side effects could be substantiated. Owing to administrative difficulties, no control groups of patients could be given streptomycin *plus* the usual régime of sodium PAS in divided doses.

Method and Material.

The sodium PAS was administered as liquid, tablets or cachets, the total dose for adults being 12 grammes of the sodium salt, which corresponds to 8·6 grammes of the free acid. The nursing staff were instructed to supervise carefully each patient taking sodium PAS to ensure that all the drug was taken in the one dose. The time during the day at which the drug was administered varied from ward to ward, but this did not significantly alter the nursing routine or incidence of toxic side effects. No patient was included in the study who was taking isonicotinic acid hydrazide, or who for any reason (for example, previous operation) was temporarily taking sodium PAS in divided doses.

The streptomycin used was plain streptomycin, dihydrostreptomycin, or a streptomycin preparation containing equal parts of plain streptomycin and dihydro-streptomycin. The dosage of streptomycin used varied, mainly according to weight (in the case of children) and the presence of complicating factors—for example, tuberculous bronchitis.

A streptomycin sensitivity test was done in all cases in which a culture of tubercle bacilli was obtained in the two months preceding the beginning of treatment. Cultural studies were repeated monthly as treatment proceeded, and each positive culture was tested for streptomycin sensitivity.

TABLE I.
Streptomycin Sensitivity Before Treatment.

Number of Cases.	Amount of Streptomycin Completely Inhibiting Growth of Tubercle Bacilli in Laryngeal Swabs or Sputum Cultures. (Microgrammes per Millilitre.)
32	Less than 0·5
1	5·0
1	10·0

These tests were carried out by the use of tubes of Dubos-Tween-albumin medium containing streptomycin in concentrations of 0·5, 1·0, 5·0 and 10·0 microgrammes per millilitre of medium, together with a control tube. The results were read in fourteen days, and the maximum concentration of streptomycin which completely inhibited growth was recorded as the streptomycin sensitivity of the culture being tested.

When three consecutive negative cultural results were obtained in cases in which they had previously been positive, these cases were omitted from the study. Although the régime of the single oral dose of sodium PAS began with 410 patients, and new patients were being added with fresh admissions, large numbers of patients were being continually taken off the study because of medical or surgical conversion of sputum, addition of izon to treatment or transfer to other sanatoria. In all the cases reported in this study a positive culture from the sputum or from a laryngeal swab was obtained at least three months after treatment was begun. No streptomycin sensitivity results are reported in children, since in no case was a positive cultural finding obtained three months after treatment was started.

Results.

Incidence of Toxic Side Effects.

In September, 1952, the number of patients in the study was 410. In March, 1953, the total was 399, and in these the total number of toxic side effects in terms of number of complaints was 119. In May, 1953, the number of patients was 383 and the number of complaints of toxic side effects had dropped to 44. In August, 1953, and February, 1954, the proportion of complaints was similar to that in May, 1953. These were of a minor nature and mainly due to gastro-mediastinal irritation. It was found that the children tolerated the single daily dose régime very well.

Streptomycin Sensitivity Studies.

Streptomycin sensitivity studies are reported in 34 adult cases of pulmonary tuberculosis. There were 18 cases of far-advanced disease, 15 cases of moderately advanced disease, and one case of minimal disease. In 25 of the 34 cases cavitation was present. Among the 25 cases in which complete inhibition was achieved by less than 0·5 microgramme per millilitre, at three months, 24 patients were receiving streptomycin, one gramme bi-weekly; 12 of these had far-advanced and 11 moderately advanced disease, and one had minimal disease. One patient with far-advanced disease and tuberculous bronchitis received streptomycin, one gramme daily, for 120 days and then one gramme bi-weekly. One patient had previously had streptomycin and sodium PAS elsewhere, and in this case complete inhibition was obtained by 10 microgrammes per millilitre

before the régime was started; the patient received streptomycin one gramme bi-weekly in this study, and at the end of three months complete inhibition was obtained by 10 microgrammes per millilitre.

TABLE II.
Streptomycin Sensitivity After the Start of Treatment.

Number of Cases.	Time when Tested.	Amount of Streptomycin Completely Inhibiting Growth of Tubercle Bacilli in Laryngeal Swabs or Sputum Cultures. (Microgrammes per Millilitre.)
25	3 months.	Less than 0·5
1	3 months.	10·0
1	4 months.	Less than 0·5
2	5 months.	Less than 0·5
1	6 months.	Less than 0·5
1	6 months.	5·0
1	8 months.	1·0
1	9 months.	5·0
1	11 months.	Less than 0·5

Of the eight patients who gave positive laryngeal swab or sputum culture findings for longer than three months after the beginning of treatment, seven received one gramme of streptomycin bi-weekly during the whole of their treatment. Four of these had far-advanced disease and three moderately advanced. The remaining patient had far-advanced disease with tuberculous bronchitis, and received streptomycin one gramme daily for sixty days and then one gramme bi-weekly.

Comments.

It has been shown by Boger and Pitts (1950) and by Bogen and co-workers (1950) that after a single oral dose of sodium PAS a peak is reached in the blood plasma in two hours, and that there is an 85% drop in four hours, due to the rapid excretion of the drug in the urine. Thus It has been thought that divided daily doses of sodium PAS are necessary to maintain an adequate concentration in blood plasma and therefore body tissues, so that the sodium PAS may exert its maximum effect in delaying the emergence of streptomycin-resistant strains of the tubercle bacillus.

It is well established that the régime of streptomycin, one gramme bi-weekly, is effective in delaying the emergence of resistant strains, as compared with the régime of streptomycin, one gramme daily. This régime must give short-lived intermittent peaks of streptomycin concentration in the blood plasma. It was therefore thought reasonable that a single oral daily adult dose of 12 grammes of sodium PAS might be just as effective as divided daily doses in further delaying the appearance of streptomycin-resistant strains.

Bridge, Carr and Karlson (1953) report a study of 14 patients with positive sputum findings at 120 days, in whose treatment the régime of a single daily dose of six grammes of sodium PAS was used, and their study suggested that this single daily dose is effective in preventing the emergence of streptomycin-resistant strains. In the present study the number of cases is small and no control group is presented. Further, no studies on the sodium PAS concentration in the blood plasma were made. Nevertheless, the study does suggest that the single oral daily dose of 12 grammes of PAS for adults is effective in delaying the emergence of streptomycin-resistant strains.

Summary.

In a sanatorium of 750 beds, an average of 400 tuberculous patients have been placed on a régime of a single oral daily dose of PAS, together with streptomycin, over a period of eighteen months. For adults the daily dose used was 12 grammes of the sodium salt.

In the past nine months the proportion of side effects in terms of complaints was approximately 11·5%; these were mainly due to gastro-intestinal irritation.

The results of streptomycin sensitivity tests on 34 adult patients with pulmonary tuberculosis are reported. If the upper limit of streptomycin sensitivity is taken as 10 microgrammes per millilitre, all 34 patients were sensitive before the régime was started.

Twenty-six patients with positive cultural findings were still sensitive to streptomycin at the end of three months; eight patients followed for varying longer periods up to eleven months were still sensitive to streptomycin.

Thirty-two patients were receiving one gramme of streptomycin bi-weekly; one patient was receiving one gramme of streptomycin daily for sixty days and then one gramme bi-weekly; one patient was receiving one gramme of streptomycin daily for 120 days and then one gramme bi-weekly.

Acknowledgements.

My thanks are due to the nursing staff of the Mountain Sanatorium for their cooperation, and to Miss F. Gray, of the laboratory staff, for performing the streptomycin sensitivity tests.

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Reports of Cases.

A CASE OF PROGRESSIVE MUSCULAR DYSTROPHY OF THE JUVENILE TYPE OF ERB IN A MAN WITH THE HISTORY OF EPILEPSY.

By O. SCHMALZBACH, M.D.,
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MR. A., aged sixty-one years, was admitted to Callan Park Mental Hospital, on November 1, 1945, as a certified patient. The following statements were made on his certificates: "Talks with a silly theatrical affectation of manner and speech and is generally foolish and irresponsible in conversation—cannot recollect recent events—so dull and confused mentally that he has not a proper appreciation of time and place." His father had died in old age; his mother is alive, aged about eighty years, and apparently healthy. There is no known insanity among his relatives. No muscular disorders have been known in the family, as far as can be ascertained, up to five generations back. The patient is the third in a family of four children. One brother died in infancy; a sister and two brothers are healthy. The patient was healthy in childhood. He was a fairly good scholar, and left school at the age of fourteen years. His employment record is of no significance; he was a flour miller for many years, and for a few years before his admission to hospital he was a textile worker. He married at the age of twenty-five years and has five healthy children whose ages range from thirty-nine to twenty-one years.

When he was aged about nineteen years the patient began to have major epileptic fits, to which he was subject for about twenty-six years. The frequency of the fits varied from one or two a week to sometimes one a day. He was treated privately. At the age of twenty years the patient noticed that his left shoulder blade protruded, and he began to feel some weakness in both

arms, particularly in the left. Approximately at that time he started to drink, and in the course of years he became a fairly heavy alcoholic. He was admitted to Broughton Hall Psychiatric Clinic twice, in March, 1931, and in December, 1940, respectively. Upon his first

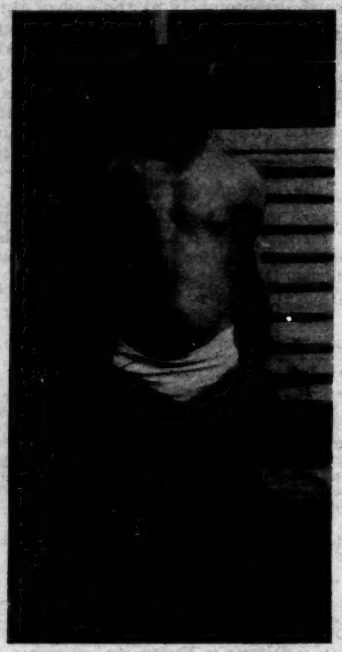

FIGURE I.

admission he gave a history of attempted suicide eighteen months previously, of epileptic fits, of weakness, and of being easily fatigued by walking; it was noticed that he showed a "muscular dystrophy". Upon his second admission to hospital he complained of progressive loss of power in both arms and had persecutory delusions concerning his wife. He was diagnosed as suffering from simple melancholia in 1931 and from a depressive state in 1940, as on both occasions he was depressed, and he was discharged from hospital, recovered, after one month and three months respectively.

Before his admission to Callan Park in 1945 the patient was involved in an accident, whilst under the influence of

FIGURE II.

alcohol, in which he was struck by a motor-car; he was admitted unconscious to the Marrickville District Hospital, where an X-ray examination of the skull failed to reveal any fracture, and no signs of subdural hæmatoma were found. However, after this accident his conduct and behaviour changed to such a degree as to make his admission to the Reception House necessary.

On his admission to Callan Park, investigation of his mental condition revealed mild confusion, impaired remote and recent memory, disorientation for time, and some degree of euphoria. No delusions or hallucinations were elicited; the patient was well behaved and quite cooperative. His mental state did not change significantly after his admission to hospital, except for some degree of secondary dementia. Physical examination of the patient revealed increased blood pressure (230 millimetres of

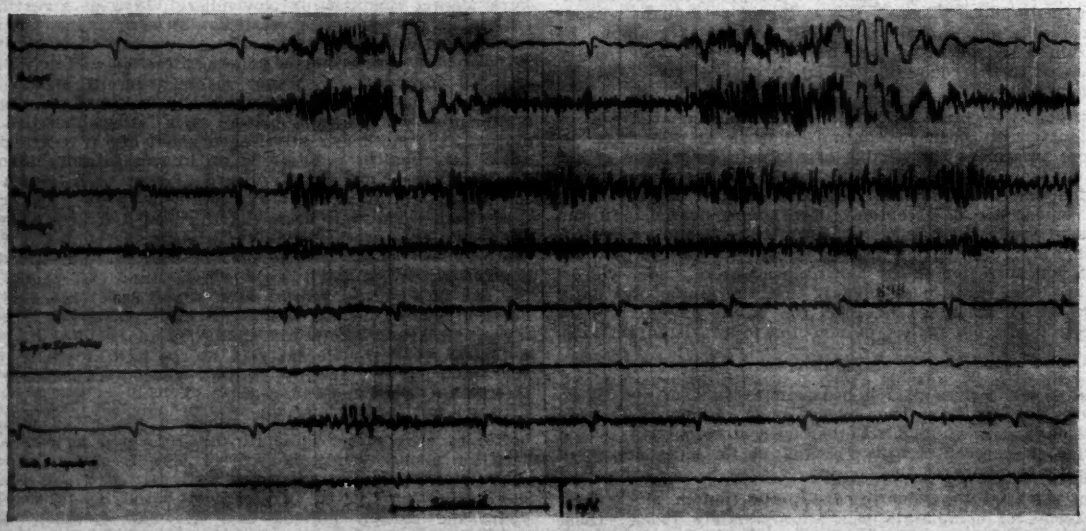

FIGURE III.

mercury, systolic, and 130 millimetres, diastolic) and thickened vessels. The cranial nerves, except for some weakness in the seventh and eleventh, were not affected. The pupils were equal; they reacted sluggishly to light and accommodation. No nystagmus was present. There was some weakness of the *orbicularis oculi* and *oris* muscles. The lower lids were drooped and the face had a hypomimic appearance (*facies myopathica*). Pain, touch and temperature sensation was normal in the distribution not only of the fifth nerve, but in the whole peripheral nervous system.

The movements in arms and shoulders were greatly diminished; as can be seen from the photographs (Figures I and II), there was considerable muscular atrophy in the scapulo-humeral region. Particularly could the atrophy be seen in the *pectoralis major*, supraspinatus, subscapularis, deltoid and biceps muscles on both sides. There were practically no rhomboids. The changes were slightly more accentuated on the left side than on the right side. (This slight asymmetry was explained by an X-ray examination of the shoulder region, which revealed an old fracture of the right clavicle.) Similar dystrophy could be noticed in the calves. The patient had pronounced lordosis and protuberance of the abdomen. His gait was disturbed—he walked on a broader base and his gait was cautious, slow and waddling. To use Kinnier Wilson's description, "He straddles as he stands and he waddles as he goes". When he moved his arms the scapulæ were winged (*scapulæ alatæ*).

The reflexes in the upper extremities were diminished owing to the muscular dystrophy, although the triceps reflexes were fairly well preserved. The knee and ankle jerks were present and equal. The plantar response was flexor in type, and no other pyramidal signs were evident. No spasticity was found in the extremities.

The Wassermann test failed to produce a reaction in the blood and cerebro-spinal fluid. No abnormalities were detected in the cerebro-spinal fluid. The Lange gold curve was represented by the figures 0011110000–00. Two electroencephalographic examinations were made in view of the history of epilepsy, and failed to reveal any abnormalities. One electroencephalographic examination was made at Sydney Hospital and one at Royal Prince Alfred Hospital; they were made independently. The last electroencephalogram was characterized by nine to ten α cycles per second; these were normally blocked on visual attention. There were no significant changes on over-breathing. On flicker stimulation there was no falling or evidence of sensitivity at frequencies from one to thirty per second. The general impression was that the record was within the normal limits.

Electromyography was carried out on the biceps, the triceps, the supraspinatus and the subscapularis muscles on both sides, and the results are shown in Figure III. It can be seen that there is inconstancy of muscle potential, indicating waxing and waning of muscular effort. Muscle potential recorded from supraspinatus and subscapularis groups was less pronounced than that usually found in normal muscles. However, this depends on the effort used during the test. No specific indication as to the type of muscle disorder can be obtained from the graphs.

Biopsy of the left deltoid was carried out at Sydney Hospital by Dr. Scott Charlton. Microscopic examination showed that most of the voluntary muscle bundles were well preserved. An occasional bundle showed degenerative changes. The cytoplasm was granular and vacuolated, and the transverse striations had been lost. Throughout the muscle there were islets of adipose tissue.

The electrocardiogram is reproduced in Figure IV. This shows evidence of myocardial abnormality.

A number of biochemical investigations were carried out. The total serum cholesterol content was 134 milligrammes per 100 millilitres (esters 98 milligrammes); the serum protein content was 6·3 grammes per 100 millilitres (albumin 3·7 grammes, globulin 2·6 grammes); the serum chloride content was 375 milligrammes per 100 millilitres (106 milliequivalents per litre); the serum calcium content was 10·1 milligrammes per 100 millilitres (5·1 milliequivalents per litre); the serum sodium content was 375 milligrammes per 100 millilitres (163 milliequivalents per litre); the serum potassium content was 21 milligrammes per 100 millilitres (5·4 milliequivalents per litre). The blood creatine content was one milligramme per 100 millilitres, and 54 milligrammes of creatine were excreted in the urine in twenty-four hours (11 milligrammes per 100 millilitres); the urinary creatinine excretion was 90 milligrammes in twenty-four hours (480 millilitres; 19 milligrammes per 100 millilitres). (It is known that creatine is not normally excreted by the adult male, but is normally excreted by children and some adult females. It appears in the urine of diabetics, in exophthalmic goitre, and in some disorders of muscle, especially muscular dystrophy.) The patient later died. A post-mortem examination of the brain and spinal cord was performed. Noticeable cortical atrophy, especially of the frontal lobes, was visible on macroscopic examination.[1]

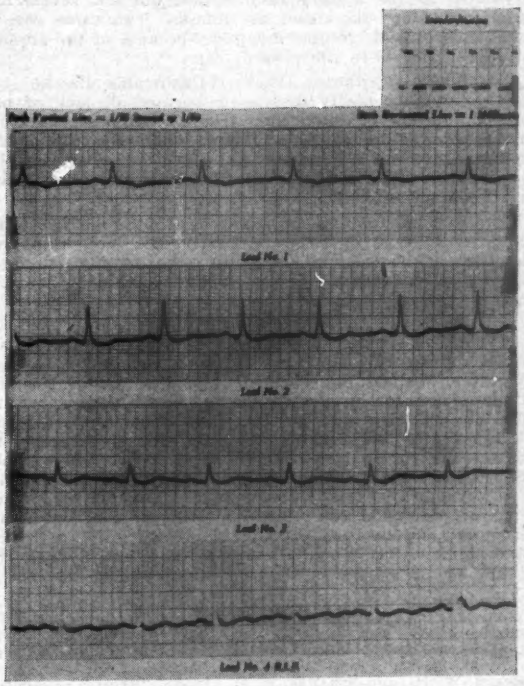

FIGURE IV.

Discussion.

In the differential diagnosis of this case one should consider progressive muscular dystrophy of Landouzy-Déjerine type. This variety belongs to the same group, and the main difference from our case is the age of onset and greater involvement of the facial musculature. The Landouzy-Déjerine type occurs earlier in childhood. In our case the symptoms started in adolescence, when the patient was aged about twenty years. According to various authors, both these types are more or less the same. Further, in the differential diagnosis one should consider lower motor neuron lesions, such as progressive spinal muscular atrophy of Aran-Duchenne type, and upper motor neuron lesions—amyotrophic lateral sclerosis or Charcot's disease. In both these clinical "entities" the first muscles involved are the small hand muscles, and fibrillations are present in atrophic muscles. In amyotrophic lateral sclerosis spasticity, particularly of the lower extremities, is a common feature and pyramidal reflexes are altered. The onset in both these types is in adult

[1] The specimen is now under histological investigation, the result of which will be reported at a later date.

life, after the age of thirty years. The Aran-Duchenne form can be a feature of various organic diseases of the central nervous system such as syringomyelia or tabes. In Charcot's disease the tendon reflexes in the arms are exaggerated and the muscle tone in the arms is diminished and that in the legs is increased. None of these features occurs in our case. Other varieties of Charcot's disease, such as bulbar palsy and nuclear ophthalmoplegia, can be excluded in this case as well.

Local post-traumatic atrophy may be ruled out in the present case because of the history and because the main characteristic of this type of atrophy is as a rule asymmetry. Again, chronic poliomyelitis can also be excluded, as the history in our case did not reveal any infection before the onset of illness. The same can be said of chronic thyrotoxic myopathy because of the absence of thyrotoxicosis in the present case.

Dystrophia myotonica (Steinert-Cushman's disease) can in this case be easily dismissed, because of lack of prolonged muscular relaxation, frontal baldness, cataract, hereditary factors and other known characteristics of this syndrome. Similarly, congenital elevation of the scapula (Sprengel's deformity) is mostly unilateral and occurs particularly in females.

The unusual features in this case of muscular dystrophy of juvenile type of Erb are, firstly, the lack of heredofamilial incidence and, secondly, the twenty-six years' history of epilepsy.

Acknowledgements.

I wish to express my thanks to Dr. D. A. S. Fraser, Inspector-General of Mental Hospitals, and to Dr. G. B. R. Wooster, Medical Superintendent of the Mental Hospital, Callan Park, for his permission to publish this report; my thanks are also due to Dr. Scott Charlton, Honorary Neurosurgeon at Sydney Hospital, for performing the muscle biopsy, to Mr. J. Davis for the electromyography, to Dr. MacDonald Critchley, Dean of the National Hospital for Nervous Diseases, Queen's Square London, for examining the patient at the clinical meeting held at the Mental Hospital, Callan Park, during his recent stay in Sydney, and to Dr. K. B. Noad, Honorary Physician, Sydney Hospital, for his advice in electrocardiography in this case.

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Social Medicine. By S. Leff, M.D., D.P.H. ("Survey of Human Biology", edited by S. A. Barnett: Number One); 1953. London: Routledge and Kegan Paul, Limited. Sydney: Walter Standish and Sons. 9" x 6", pp. 310, with about 20 graphs. Price: 28s.

THE author of this book, who is both a medical practitioner and a barrister-at-law, has designed his book for both medical and non-medical readers and has gathered together a great deal of information which he has centred round the concept that he has of social medicine. After an introductory discussion on the meaning of social medicine and an historical sketch to provide a background, he devotes chapters to methods of research, infectious diseases, death rates, housing and health, nutrition, conditions of work, tuberculosis and society, rheumatism, mental disorder, the care of the aged, social medicine and war, and the health of the Services. Much of the book is dull and heavily factual, but those who are interested in the subjects listed or in the question of social medicine as a whole, will find a good deal here to interest them.

Clinical Endocrinology. By Karl E. Paschkis, M.D., Abraham E. Rakoff, M.D., and Abraham Cantarow, M.D.; 1954. New York: Paul B. Hoeber, Incorporated. 9½" x 6½", pp. 842, with 253 illustrations, five in colour. Price: $16.00.

IN this book the authors have given a comprehensive account of the endocrine glands and their diseases. The book represents a synthesis of the experiences and interests of the three authors in physiology, clinical endocrinology and biochemistry. As a result of their cooperation the subject matter has been presented in a uniform style without unnecessary overlapping.

The book is divided into twelve sections dealing respectively with the anterior lobe of the pituitary, the posterior pituitary lobe, the thyroid gland, the adrenal cortex, the adrenal medulla, the ovaries, the placenta, the testes, the pancreas, the parathyroids, obesity, and finally in the twelfth section with laboratory procedures and methods of study used in the investigation of the functions of the glands. A list of hormone preparations produced by the various commercial houses is appended. In each section the anatomy and physiology of the glands are described and conditions in which function is overactive or depressed are discussed. A full bibliography is appended at the end of each section. The book is well illustrated and there is a good index.

The authors stress the point that the foundations of our knowledge of endocrinology were laid by clinicians. This, of course, is largely true and should be borne in mind by all investigators. The authors in this regard quote the work of Pierre Marie, Gull and Addison, master clinicians of the last century, and of Albright of more recent times.

There are various minor criticisms such as the omission of reference to that important milestone in endocrinology, the pioneer work of G. R. Murray in the treatment of myxœdema by means of thyroid substance administered orally, and the appearance of the portrait in Figure 50 which is entitled "Myxedema", but is not a typical example of the disease.

The book can be recommended to any practitioner interested in the endocrine glands and their diseases in search of a comprehensive account of the subject.

The Anatomy of the Eye and Orbit: Including the Central Connections, Developments, and Comparative Anatomy of the Visual Apparatus. By Eugene Wolff, M.B., B.S. (London), F.R.C.S. (England); Fourth Edition; 1954. London: H. K. Lewis and Company, Limited. 10" x 7½", pp. 500, with 406 illustrations, 52 in colour. Price: 63s.

WHEN Eugene Wolff's "Anatomy of the Eye and Orbit" was first published in 1933 it was a volume of 300 pages with 178 illustrations. By 1951 three editions and seven reprints had been required, as it had established itself as the standard text-book for post-graduate ophthalmology students and their teachers. Practising ophthalmologists had found it a valuable reference book, and the outstandingly clear and informative illustrations had been borrowed by the writers of many ophthalmic papers and text-books.

The fourth edition has now appeared (1954), but unfortunately it will be the last that will be written entirely by its originator, because Eugene Wolff died suddenly a few days after his passing the final proofs. The new edition has 492 pages and 406 illustrations, of which 52 are in colour. Compared with the third edition this is an increase of 50 pages and 83 illustrations including 28 more coloured plates. The main changes and additions are in the description of the canal of Schlemn, where the discovery of Pacchionian bodies in its inner wall is mentioned; of the limbus; of the difference between the medial and lateral sides of the eyelids; of the optic tract; of the commissure of Gudden and the lateral geniculate body; of the blood supply of the third, fourth and sixth cranial nerves; of the development of the vitreous and the normal appearances as seen with the gonioscope.

The general production is of the same high standard as that attained by previous editions. The blue cover with gold lettering is very attractive, but unfortunately this colour tends to fade when exposed to light, and after a time on library shelves the title loses its prominence and becomes difficult to see.

This anatomy book needs no recommendation, as its reputation has been firmly established. Post-graduate ophthalmology students are fortunate in having such an excellent book to read, and the prestige of British ophthalmology has been considerably enhanced by this publication of Eugene Wolff.

A Manual of Otology, Rhinology and Laryngology. By Howard Charles Ballenger, M.D., F.A.C.S., and John J. Ballenger, B.S., M.S., M.D.; Fourth Edition; 1954. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9½" x 6½", pp. 366, with 139 illustrations, three in colour. Price: 64s. 6d.

AT first sight the "Manual of Otology, Rhinology and Laryngology", by Howard Charles Ballenger and John J. Ballenger, appears to be a small standard text-book of conventional type with particularly good simple black-and-white illustrations and the usual batch of alternating pallid and overdone colour illustrations which help the reader little but greatly increase the depth to which he must delve in his pocket to purchase a copy.

The authors state that the book is written primarily for the undergraduate medical student, but add a hope that it may be of use to non-otolaryngologists and otolaryngologists.

The appeal of the manual appears to be very limited because surgical treatment is either omitted altogether or is dealt with so scantily as to make it unsuitable for the undergraduate who owns only one book on the subject; whilst the otolaryngologist is unlikely to consult it for reference, except for matters anatomical which are dealt with surprisingly well and thoroughly, considering in how many other aspects the book has been condensed.

If the authors' indications for tonsillectomy are accepted the operation may be performed, if such is possible, even more often than it is today, for on page 133 they state: "Malnutrition in children in the absence of other cause may be considered an indication", whilst on page 125 appears the statement: "In the chronically ill, typically healthy tonsils are the exception rather than the rule."

The style of writing is free from Americanisms except for the startling spelling of "Maneuver" on page 230.

It is a pity that somewhat loose thinking allows frequent and annoying repetition of advice to use as treatment "the sulphonamides and/or the antibiotics".

In spite of excellent printing and binding, excellent black-and-white illustrations, excellent handling of various subjects beside that of anatomy, and lastly, in spite of the book's being written by such talented authors who have produced larger text-books of undoubted proven value, one cannot but feel that their attempt to provide a condensed one "misses out", because it does not provide exactly what any one large class of reader requires.

A Synopsis of Anæsthesia. By J. Alfred Lee, M.R.C.S., L.R.C.P., M.M.S.A., D.A., F.F.A.R.C.S.; Third Edition; 1953. Bristol: John Wright and Sons, Limited. 7½" x 5", pp. 492, with 72 illustrations. Price: 21s.

THE third edition of Lee's book will be welcomed by all anæsthetists. The synoptic style and handy format of the edition of 1950 have been preserved, but the illustrations continue to depict mainly the exterior of apparatus and are therefore of but little value. The present edition is longer than its predecessor by 130 pages. This increase is due, in part, to two new chapters. Of these, one deals with induced hypotension and is judicial in its approach to the subject. The other, upon the therapeutic aspects of anæsthesia, shows how the anæsthetist can assist his colleagues of other specialities in such problems as the relief of intractable pain or the management of pulmonary œdema; it forms a brief but suggestive introduction to a vast field.

In the main, however, the expansion of the text results from careful revision of almost all sections, whether anatomical, physiolcgical or clinical. The more significant publications, up to the year 1953, are cited and accounts are given of such recently introduced drugs as "Efocaine", n-allyl normorphine, noradrenaline and the depolarizing relaxants. The end result is a topical volume, which deals with such current questions as the management of adrenalectomy or the incidence of retrolental fibroplasia in premature babies.

Despite its modernity, the work carries over from previous editions a number of questionable practices. It still advocates partial rebreathing and the administration of carbon dioxide for the speeding-up of anæsthetic induction. It cites a technique for the administration of nitrous oxide for minor dental operations, which employs 6% to 10% of oxygen. It describes distension of the breathing-bag as a practical, though belated, sign of accumulation of carbon dioxide in an absorption system. It repeats the statement, made in the previous edition, that, since the general use of relaxants, the need for tracheal intubation has decreased: we are of directly contrary opinion. Pulmonary hyperventilation is said to be seldom harmful: this may be the case in healthy subjects, but certainly not in those suffering from pyloric obstruction or other states of alkalæmia.

In a volume otherwise encyclopædic, space might well have been found for clear-cut essays upon anatomical and mechanical dead space, and upon the relative merits, defects and applications of "controlled" and "assisted" respiration. The account given of replacement therapy halts, in the main, at sodium chloride and water; it might have been extended usefully to the other factors which appear upon Gamble's chart. Finally, the author's views would have been welcome upon that much-discussed question of the moment, namely, rapid resuscitation and early operation for the removal of shock-producing factors.

In previous editions the author presented a great variety of methods for the solution of a given problem in anæsthetics, citing his authorities, but making little attempt to indicate his personal preference. He now allows his own views to become more evident: indeed, we could wish that he had done so uniformly, because his opinions are such as command respect. As it stands, however, his book is better suited to the experienced anæsthetist than to the novice. The former will find it a valuable summary of the literature and a compendium of alternative methods; the latter may have difficulty in choosing between the great variety of well-sponsored techniques which is presented for his choice.

Lectures on General Pathology: Delivered at the Sir William Dunn School of Pathology, University of Oxford. Edited by Sir Howard Florey; 1954. Melbourne: Melbourne University Press. 9½" x 6½", pp. 748, with 344 illustrations and four colour plates. Price: 84s.

THIS is a beautifully produced and lavishly illustrated volume, incorporating a series of 37 lectures on general pathology by ten authors. It does not attempt to cover the entire field, for though there is a central theme, the choice of subjects has been at least partly determined by the special interests of researchers currently working in Oxford; nine of the authors are Oxford men. This is all to the good, for each thus writes with special authority in his own field. It perhaps explains, however, the most notable omission, for tumours are not considered at all. It is to be hoped that in future editions it may be possible to rectify this.

The series is based on the twin beliefs that nowadays general pathology is a science in its own right—and a very difficult one—and that few significant advances in general pathology can hereafter be expected from the application of the conventional methods of morbid anatomy. The emphasis is in consequence on the functional and experimental approach to the subject, to show not only what is the present state of knowledge, but also how it has been obtained. Each lecture is thus very detailed and is followed by a lengthy list of references, and a praiseworthy effort has been made to provide an historical background to each. As might be expected, the lectures vary a little in quality. Some are first rate; for example, those on the fundamentals of inflammation, in which the extensive observations of the Oxford school on inflammatory reactions in thin living tissues are brought together, to the virtual exclusion of those derived from the time-honoured but much less satisfactory fixed and stained sections. Anyone who has studied these beautiful living preparations will never again be entirely satisfied with conventional techniques. It is good here to see that due regard is paid to the similar observations on living membranes made by English workers a century ago, which had been rather lost sight of, and to which, all things considered, not very much has since been added. However, it is a great pity that the chapters on repair are separated by some hundreds of pages from those on inflammation. The experience of most teachers is that these two topics fall naturally together.

The lecture on degenerations is very scrappy and disappointing, but the several lectures on immunology are particularly good, providing a mass of detailed information without attempting to hide the complexities. Indeed the

simple things are assumed, for the common pathogens are not described, and Gram's stain is not mentioned. Again we would have preferred a little less detail of the chemical complexities of blood coagulation and some mention of the more mechanical and anatomical effects of thrombosis, for infarcts also are not considered. In fact we wonder whether these lectures would have had quite their present form and content if the lecturers had later to follow up with a course in special pathology, as is the lot of most teachers. Among other good chapters are those on the effects of radiations on cells, and on the cellular and tissue reactions to viruses, though it is odd in the latter chapter, in a book with so much that is new, detailed and exciting, to find no mention of Burnet's work. The chapters on antibiotics are naturally especially authoritative.

We are told that these lectures are intended for the better student. Certainly they will bewilder the merely average one, as they are at once too detailed for him, cover only a portion of the subject, and do not integrate well with the later work in the wards, the autopsy room and the museum. The integration of fundamental with applied pathology is, of course, a very difficult business, and with advancing knowledge, as this book shows, is not likely to grow easier. This book will be most useful to post-graduate students, and especially to the small but growing circle of academic professional pathologists with experimental inclinations. It is an important milestone on the road to the establishment of general pathology as a science in its own right, and shows that to cover the whole subject in the fundamental manner here used would require a multi-volumed work and an international team of contributors. After all, it is not to be expected that the fundamentals of pathology will turn out to be simple, though they are still sometimes taught as if they were.

Twenty-Five Years: The Story of the Royal College of Obstetricians and Gynæcologists, 1929–1954. By William Fletcher Shaw, M.D., F.R.C.P., F.R.C.O.G., Hon. LL.D.; 1954. London: J. and A. Churchill, Limited. 8½" x 5½", pp. 100, with 17 illustrations. Price: 21s.

TODAY the Royal College of Obstetricians and Gynæcologists is respected and consulted not only by the community at large, but by the other two ancient Royal Colleges which first so firmly opposed its foundation. Indeed, admission to its membership has become almost a *sine qua non* for aspiring consultants in obstetrics and gynæcology throughout Britain and the Empire. No man is better able to describe this remarkable achievement than Sir William Fletcher Shaw, first Secretary of the College and President from 1938 to 1943. One of the first men to recognize the necessity for a College in the early 1920's and to elucidate its fundamental objectives, he belonged to that small band of zealots which included Blair Bell, Ewen Maclean and Comyns Berkeley. Their imagination, drive and wisdom were to rally support and to underpin the College structure in its uncertain beginnings. From his own memory and the official correspondence Fletcher Shaw has drawn most of his material. During the last three decades his friendship and personal contact with the outstanding men in the College have enabled him to trace the influence of their differing personalities on the direction which the developing College took from William Blair Bell, its first, to Arthur Gemmell, its current President. To the whole task the author brings a clear, incisive mind and an attractive informal literary style. The result is a well-illustrated book which gives a lively and penetrating account of the Royal College of Obstetricians and Gynæcologists in its first twenty-five years.

Basic Anatomy. By G. A. G. Mitchell, O.B.E., T.D., M.B., Ch.M., D.Sc., and E. L. Patterson, M.D., Ch.B., B.Sc.; 1954. Edinburgh and London: E. and S. Livingstone, Limited. 10" x 7", p. 446, with 286 illustrations. Price: 45s.

THIS is a book "based on an introductory course of lectures for medical and dental students". The authors have had several aims in view, but the chief of these are:

(a) To bring basic information about human anatomy and to synthetize facts from various subjects into a story which may serve as a bridge between Biology, Anatomy, Physiology and clinical subjects.

(b) To attempt to explain briefly how man is evolved and developed. . . .

(c) To provide an epitome of the main facts about the various bodily systems. . . .

The authors appear to have a sound knowledge not only of anatomy and related subjects, but also of their clinical applications. The book is extraordinarily well printed, the type is easily readable, and the illustrations are very clear. The photographs and photomicrographs are very good indeed.

There is a very satisfactory brief chapter on the history of anatomy, including illustrations of Harvey's experiment to demonstrate the venous valves and the direction of the blood flow.

The authors point out that anatomy means far more than the study of the dead and "much of importance may be discovered by studying the Anatomy of the living by investigating the derangements produced by injury or disease, and by exploiting such aids as X-rays to reveal some of the hidden secrets of the body. . . .".

In the chapter on joints, two very short paragraphs emphasize the importance of the blood supply and lymphatic drainage. Attention is drawn to Hilton's law, that the nerve supply in the joints supplies also the muscles moving the joint and the skin over the insertion of the muscles. A very good account is given of the spinal movements and mechanics.

The nervous system is particularly well dealt with and the more recent advances have been noted, for example, "certain nerve cells in the hypothalamus contain colloid material which may pass into the blood and get like the hormones produced by the endocrine glands". "The chief autonomic centres are in the frontal lobes of the brain . . . and the integration of somatic and autonomic activities enables the body to maintain suitable internal conditions despite changes in the external environment."

This work is a fine example of the modern approach to anatomy, and is recommended to students and practitioners.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Proceedings of the First World Conference on Medical Education, London, 1953: Held under the Auspices of the World Medical Association"; 1954. London: Geoffrey Cumberlege, Oxford University Press. 9¼" x 6¼", pp. 820. Price: 60s.

Contains the papers in the language in which they were presented, and also the main points in the discussion. The editor is Dr. Hugh Clegg, editor of the *British Medical Journal*.

"Cerebrovascular Disease", by James Peter Murphy, M.D., with a foreword by Percival Bailey, M.D.; 1954. Chicago: The Year Book Publishers, Incorporated. 9" x 6", pp. 408, with 128 illustrations. Price: $12.00.

The author is stated in the foreword to be "a neurological surgeon with an extensive basic training in the anatomy, physiology and pathology of the brain".

"The Year Book of Medicine (1954-1955 Year Book Series)", edited by Paul B. Beeson, M.D., Carl Muschenheim, M.D., William B. Castle, M.D., Tinsley R. Harrison, M.D., Franz J. Ingelfinger, M.D., and Philip K. Bondy, M.D.; 1954. Chicago: The Year Book Publishers, Incorporated. 8" x 5¼", pp. 712, with 115 illustrations. Price: $6.00.

One of the Practical Medicine Series of Year Books.

"Illustrated Handbook of Child Care from Birth to Six Years", compiled and illustrated by Wava McCullough, assisted by Marcella Gawronski, R.N.; 1954. New York: McGraw-Hill Book Company, Incorporated. 9¼" x 6¼", pp. 240, with about 400 illustrations. Price: $4.00.

A book of directions to mothers in the care of their babies—the illustrations are first rate.

"Heart: A Physiologic and Clinical Study of Cardio-vascular Diseases", by Aldo A. Luisada, M.D., with a foreword by Herrman L. Blumgart; Second Edition; 1954. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" x 7", pp. 694, with 312 illustrations. Price: £8 1s. 3d.

Written for "the large group of physicians who desire to increase their knowledge of heart disease".

The Medical Journal of Australia

SATURDAY, DECEMBER 11, 1954.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

INTERNATIONAL STANDARDIZED ANATOMICAL NOMENCLATURE.

At long last there appears to be some good hope that anatomical nomenclature will be modernized and standardized for international usage. In 1895 a group of German anatomists, with some help from others, brought out the *Basel Nomina Anatomica*, known widely as BNA. This was adopted by several countries, including the United States of America, but Britain was never wholly committed, whilst in France and other Latin countries its reception was particularly cool. In 1933 the Anatomical Society of Great Britain and Ireland published a review of the BNA which included many improvements. At about the same time a German commission prepared the *Jena Nomina Anatomica (JNA)*. This scheme was very radical, especially with respect to terms indicating direction and situation, abandoning the conventional anatomical position which suits the quite anomalous posture of the human body and bringing in "caudal" and "cranial" for "inferior" and "superior", also "dorsal" and "ventral" for "posterior" and "anterior", changes which were welcomed by the biologist and also the physiologist, whose experimentation is largely concerned with the lower animal. An international congress was planned to be held in 1940, and the American Association of Anatomists took great pains in examining the whole position and preparing its own list. Unfortunately the outbreak of the second World War led to the abandonment of this congress, and the BNA continued to be used in the United States of America. In 1950 a congress was held in Oxford, and it there became apparent that German, Dutch and Scandinavian anatomists who used the Jena system were not satisfied with that and demanded a reform. The American and Canadian committee after prolonged study had come to the conclusion that a modified revision of the BNA would meet all requirements; while the British, finding that their version of the same system, abandoning excessive Latinisms, was working well, expressed their willingness to help in an international revision of the BNA. The president of this congress, Professor Le Gros Clark, formed a 30-member international committee, which elected a smaller executive committee representing South America, France, Italy, Sweden, Germany, Holland and Britain with an American as secretary. Somewhat significant was the action of Russia, which never even acknowledged the receipt of the invitation though correctly sent through diplomatic channels. Through the hospitality of the Ciba Foundation the executive committee met in London in 1952 and agreed completely on general principles. The work of revision was entrusted to seven subcommittees made up of 23 anatomists representing 10 countries. The drafts then prepared were extensively revised and edited at a second London meeting of the executive committee in June, 1954. At this meeting some useful suggestions were contributed by the Japanese anatomist Ogawa, of Tokyo. The final draft will be submitted to the next congress to be held in Paris on July 25 to 30, 1955, and it is confidently expected that unanimity will be reached.

Of course, it is impossible that everybody interested will be pleased; perhaps the decision which will cause most regrets, especially amongst the older surgeons, is the unanimous exclusion of eponymic titles. No longer are we to use Scarpa's triangle or Poupart's ligament, islands of Langerhans, nodes of Ranvier or circle of Willis. No doubt a bid for immortality has been made on behalf of anatomists whose contributions to the science have been unimportant, and so to stop this abuse all eponymic titles are to be abolished. One has frequently heard that the opposition of German anatomists to proper names in terminology arose from the paucity of Teutonic names in the science. If trouble be taken to classify the names in the index of a text-book of anatomy, it will be seen how grossly untrue this suggestion is, for such names, excluding a few of Hebrew origin, far outnumber those of any other race. It is a pity that this drastic reform is to be made retrospective, and honoured names in discovery are to be jettisoned. A limiting date could have been chosen, say 1850, and the assigned names before this year retained on account of their long association. Another objection is that at present teachers of science in general are anxious that students should know a little more than they do of the history of each specialty, and the retention of illustrious names is a certain method of stimulating interest in this branch of the subject. There would unquestionably be a violent protest if it was suggested that mathematics and physics should follow this lead and renounce all eponymic titles, for from Archimedes to Heaviside there is a series of names of brilliant thinkers, inventors and experimenters, each of whom shed glory on his subject and his country. It may perhaps be not too late to hope that some compromise may be reached respecting the imposition of so

severe a measure. The deductive and severely logical analysis of mathematics has its human side, and much more so has animal morphology, and this aspect should not be lightly overlooked.

Current Comment.

A REPORT ON MATERNAL AND BABY WELFARE.

FROM August, 1950, to March, 1951, Dr. Grace J. Cuthbert-Browne, the Director of Maternal and Baby Welfare of the New South Wales Department of Public Health, made a study overseas, as a World Health Fellow, of maternal and child health. The Department of Public Health of New South Wales has issued a lengthy report on her findings. This is a document of some 273 pages of single-spaced typing, reproduced on the roneo and bound. The report is divided into three sections. In the first section, brief comment is made on the outstanding problems and topics in the field of maternal and child health. In the second section, some eleven subjects are dealt with at considerable length, and in the third section, the services available for mothers and children and the administrative techniques practised in the following countries are discussed: the United States, Canada, Norway, Sweden and Finland.

In this place it will be sufficient to set out the main conclusions and recommendations of the report; those who wish to study the matter in greater detail are referred to the report itself. The first set of recommendations are described as national. This means that they could be implemented with the assistance of the Federal Government. The second group of recommendations relates specifically to the State of New South Wales.

The first of the national recommendations is to the effect that a policy of grants-in-aid for approved programmes for the care of mothers and children and for crippled children's services, including the day care of children under school age in all States, should be adopted by the Federal Government. In order to implement this, it is stated that the Federal Government would require each State to provide: (*a*) a statement of its activities for maternal and child health and crippled children's services, including nutrition and health education and plans concerning these; (*b*) a statement of projected activities at present in abeyance on account of the lack of funds, lack of staff, or both. It is stated that the Federal Government should also provide funds to each State for the extension of existing schemes and the establishment of additional services. These funds should be available as an equal basic annual grant increased by such factors as: (*a*) the number of births in each State related to the total Australian births; (*b*) the rurality of the State; (*c*) the total area of the State; (*d*) special needs of the States, particularly those due to difficult climatic and geographic conditions affecting transport and living conditions. The final national recommendation is as follows: "The provision of Federal health education materials for maternal and child health and crippled children's services, including nutrition and dental health education."

The first recommendation related specifically to the State of New South Wales is for the appointment of an advisory medical committee on maternal welfare to advise on the extension of services and to ensure the cooperation of the medical profession and the Hospitals Commission. Dr. Cuthbert-Browne thinks that the basic representation on such a committee should be as follows: (*a*) Hospitals Commission, (*b*) Royal College of Obstetricians and Gynæcologists, (*c*) the Professor of Obstetrics of the University of Sydney, (*d*) representatives from the teaching hospitals, (*e*) a representative from the Section of Obstetrics and Gynæcology of the New South Wales Branch of the British Medical Association. Dr. Cuthbert-Browne thinks that pre-natal care could be improved by the adoption of the following nine measures: (i) The extension of facilities for pre-natal clinics to areas outside the metropolitan area with provision of a fee *per capita* payment to the medical practitioners supervising the clinics. (ii) Free consultant advice during pregnancy to areas outside the metropolitan area. (iii) Free services for routine hæmatological examinations and routine thoracic X-ray examinations when patients cannot afford to pay (these, it is stated, can be arranged in Sydney). (iv) Free service for kidney function and other tests when patients cannot afford to pay (these, it is stated, can be arranged in Sydney). (v) The Department of Labour and Industry and Social Services to be asked to accept the policy of home help service as an essential requirement for expectant mothers during the last four weeks of pregnancy. (vi) The encouragement of the extension of home help service by increased publicity and the provision of more funds to include the establishment of hostels for the employees, and a training school. (vii) The provision of sufficient beds for adequate supervision of the complications of pregnancy. (viii) The provision of physiotherapy services for mothers attending pre-natal clinics by part-time or fee *per capita* payments. (ix) The provision of improved health education including child development *et cetera* for expectant mothers.

For the improvement of lying-in care, the following five measures are recommended: (*a*) The extension of the free consultant services to the remainder of the State for mothers who cannot afford to pay or whose location makes it impracticable. (*b*) Extension of mobile blood transfusion facilities to the remainder of the State by cooperation with the base hospitals and the Red Cross Transfusion Service. (*c*) Provision of adequate beds to ensure the early admission at all hospitals of patients suffering from miscarriage and abortion. (*d*) The provision of additional obstetric beds to ensure an adequate period in hospital for the mother after the birth of the baby. (*e*) The extension of the investigation of maternal deaths to the remainder of the State.

Dr. Cuthbert-Browne recommends the appointment of a pædiatric advisory committee to advise on matters concerning extension of services and care of premature babies, or matters such as infant feeding, and to ensure the cooperation of the medical profession. She thinks that the basic representation on such a committee should be as follows: (*a*) The Institute of Child Health, (*b*) The Royal Society for the Welfare of Mothers and Babies, (*c*) The Royal Alexandra Hospital for Children, (*d*) The Australian Pædiatric Association, (*e*) the section of pædiatrics of the New South Wales Branch of the British Medical Association. She remarks that the present policy of the Department of Health "in depending on the remote control of the Honorary Medical Staff of the Mothercraft Training Schools of the Royal Society for the Welfare of Mothers and Babies for the standards of infant feeding and other pædiatric practice, is no longer tenable". She states that since her return from overseas, she has made a special endeavour to obtain a balanced and acceptable opinion on infant feeding and management to guide the nursing staff of the Baby Health Centres. The wide variation in practice and opinion existing within the honorary medical staff itself, and the deviation of the teaching at the training schools where the Baby Health Centre nurses are trained, and the teaching at the Institute of Child Health of the medical students who make observation visits at the Centres, make it impracticable to continue to accept this remote control.

In Dr. Cuthbert-Browne's opinion, infant welfare nurses should be registered, and the requirements for the training of Baby Health Centre nurses should be broadened, as in Queensland. She thinks that the recruitment of infant welfare nurses should be encouraged by the alleviation of hardships due to travelling and/or climatic and geographic conditions in Sydney and the remainder of the State by several methods. The first is free transport to the city four times a year—for recreation, at Christmas, at Easter

time, and on one other public holiday—for all nurses stationed more than 100 miles from their home town or from Sydney, and twice a year for those located over 50 miles distant, similar to allowances made in Victoria. The second is by the reimbursement of all fares in excess of those for six miles from Head Office in the metropolitan area. The third is by the payment of the cost of a motor-car of suitable type for the district to the Municipal or Shire Council, together with depreciation and mileage allowances, to provide transport for the sister while she is on duty, as is done in Victoria. Other methods suggested for the encouragement of recruitment include the offering of more opportunities for promotion by the following methods: (*a*) The creation of a nursing position at Head Office to effect liaison between the maternity hospital and the department on the care of premature babies, and the follow-up service in the home. (*b*) The creation of one special position in each health district to provide additional liaison with Head Office, and a pre-school advice service to the Baby Health Centres in the district. (*c*) The provision of a special financial allowance for three years' country service to increase progressively for each hundred miles distant from Sydney. (*d*) Increased rates of pay to remunerate nurses for additional training.

It is recommended that additional mothercraft homes should be provided at such towns as Goulburn, Orange, Armidale, Wagga Wagga and Young.

Dr. Cuthbert-Browne thinks that still births and premature births and neonatal mortality could be reduced by the following measures. (i) The acceptance of the definition of a premature infant as one whose birth weight is five and a half pounds or less. When the weight is not specified or obtainable, a live born infant of less than thirty-seven weeks' gestation should be regarded as premature. (ii) The prevention of premature births by: (*a*) Improved pre-natal care by extension of pre-natal clinics in Sydney and by the establishment of similar clinics in the health districts, beginning with Wollongong and Newcastle, where practicable. (*b*) More intensive health education of the expectant mother in nutrition and child development and management of newly born babies and physiotherapy services. (*c*) The provision of more home helps for New South Wales. We read that in addition to malnutrition, it is felt by many authorities that want of sufficient rest in the last six weeks of pregnancy may be an important factor in causing premature birth. Therefore, an extension of the home help scheme and the provision of help before the baby is born are recommended.

Legislation, in Dr. Cuthbert-Browne's opinion, should be undertaken for the notification of eclampsia, the notification of all premature births with provision for necessary information concerning mother and child, the standardization of nurseries for the newly born in regard to the care of and admission to hospital of premature babies. She thinks that properly constructed premature carriers should be provided at all ambulance stations for the conveyance of babies as required. She also recommends the provision of a follow-up nursing service for premature babies and the provision of more mothercraft homes in New South Wales, so that premature babies in areas outside Sydney will have a better chance of survival.

Dr. Cuthbert-Browne thinks that an inquiry should be undertaken in regard to all deaths of infants under one month, the object to be (*a*) the comparison of the neonatal deaths in proportion to the number of confinements taking place at the various hospitals; (*b*) the relation of the facilities for the care of the newly born to the number of deaths; (*c*) the circulation each month to all hospitals of the list of hospitals with the number of neonatal deaths per month; (*d*) the classification of the cause of death.

The last recommendation deals with the day care of children under five years of age. Here we see recommended: (*a*) the establishment under the Department of Health of a day care unit representing those organizations now taking part in the provision of day care services and receiving government subsidy; (*b*) the provision of funds on a *per capita* basis as in Victoria; (*c*) the recognition of the need for smaller units and part day services to meet the severe staff shortage to reduce the cost of the service; (*d*) the establishment of a short course of training to Baby Health Centre nurses, so that in country districts advice on problems of this age group can be offered at Baby Health Centres; (*e*) the provision of part-time services of mature experienced nursery school teachers to advise mothers on problems of this age group at special sessions.

From the foregoing it will be seen that Dr. Grace Cuthbert-Browne has made a most complete set of recommendations. It is hoped that this report of hers will not be pigeon-holed, but that at least some of her recommendations will be accepted and that administrative action will follow.

THE MALNOURISHED COMMUNITY.

THE distribution and availability of foodstuffs among the peoples of the world are very uneven and a large proportion of the world's population is undernourished. With the growth of nationalism, particularly in Asia and Africa, there is an increasing awareness of the plight of the underprivileged people and of the part which must be played by the more privileged people to correct the position even if only from the point of view of self interest. Much is being done to improve the economic position of the people and, directly and indirectly, to improve the nutrition. Many of the developmental schemes which are in operation are on a large scale, and some years will elapse before the benefits accruing from them will be very apparent. Smaller schemes on a village level offer opportunities for getting quick results with relatively small expenditure of money. B. S. Platt,[1] who has done considerable work on the improvement of nutrition and hygiene among the poorer people in various parts of the world, suggests that the best starting point for such schemes would be to introduce measures designed to improve the health and welfare of mothers and children. Improvement of the health of women would immediately lead to increased capacity to work and therefore to improved production of foodstuffs. It is to be remembered that in underdeveloped countries the greater part of the production, processing and preparation of foods is done by women, and anything which will improve their capacity to do these things will improve the food position and so the nutrition. Many of the larger developmental schemes are concerned with the production of crops for export by the men with the aid of modern methods and appliances of agriculture. The better techniques should also be made available for the women for the production of food crops for domestic consumption.

It is obvious that any scheme to be successful must be acceptable to the people and must not too much upset their social customs and way of life. Attempts to impose measures successful in European countries on coloured people in the tropics have often had unsatisfactory and sometimes unfortunate results. The general aim should be preventive—that is, to avoid political, social and economic as well as medical ills, rather than to rescue casualties in these fields, as has been the case in the past. Measures directed towards the improvement of health and conditions of women and children will have an emotional appeal, so that they are likely to be taken up and the people's cooperation secured. Welfare work among women and children will help materially in the solving of one of the greatest problems in tropical countries—the alarmingly high infantile and maternal death rate. Infantile death rates as high as 500 per 1000 are not uncommon; and even when they are much lower than this, deaths in early childhood reduce the number of survivors to reach adult age to half or fewer of the number of births. Backward people usually have many children, so that some shall survive to support their parents in their old age.

[1] *Lancet*, November 6, 1954.

This means very frequent pregnancies, and these with the poor hygiene and the general malnourished state of the mothers lead to a high maternal mortality. Diseases like malaria, of course, also are important in the high infantile and maternal mortality, but these are being overcome.

An immediate consequence of better feeding of the mother would be that she would produce milk in ample quantity and for a prolonged period of lactation. It is a very general custom in these countries for children to receive breast milk for two years or more; this has the advantage that the children get a better protein than they would generally if weaned early, even if in inadequate amounts, and pregnancies tend to be not too close together. Until the general nutrition is increased improvement in the mother's nutrition will give more first class protein for the infant and young child and so contribute to the eradication of protein malnutrition in children, which is widespread and serious. The prolonged period of breast feeding under these conditions is better than the introduction of cow's milk, when it can be got, or of substitutes, such as soya milk, which it would be difficult to keep under the hygienic conditions existing. Platt suggests that it would be well, for the time being at any rate, to confirm women in their role of food producers and to band them together into useful social units, such as the Women's Institutes of England. This latter move would help to raise the status of women in society. He emphasizes the need for tempering "the urge towards innovation with the legitimate restraints of custom". To make such a programme successful some provision would have to be made for the increased availability of protein foods to supplement the vegetable food grown in the villages. This is a basic problem for most countries. In India and in Indonesia this problem is being met in part by a large increase in supplies of fish. In other Asian countries greater use is being made of soya beans, peanuts and pulses.

The large increases in population in Asian countries, which will arise from these and similar methods for the improvement of nutrition, as well as the lessened incidence of tropical diseases with improved hygiene, will raise new problems of food supply, and Australia will certainly be called upon to supply much more food in the near future.

A NEW TEST FOR PANCREATIC FUNCTION.

LABORATORY TESTS for pancreatic function in cases of suspected pancreatitis have not proved very satisfactory. A gelatin tolerance test has been used, depending on the assumption that as trypsin plays an important part in the hydrolysis of proteins in the gastro-intestinal tract, the blood amino acid nitrogen level will not rise so high after a protein meal when trypsin is deficient as it does in the normal person. This test has not proved very reliable, for there is a great deal of overlapping between normal and abnormal subjects.

T. L. Althausen and K. Uyeyama have devised a test based on starch tolerance.[1] Very little digestion of starch is brought about by ptyalin; by far the greater part depends on the action of pancreatic amylase. The test is carried out as follows. One hundred grammes of "soluble starch" (Lintner) are suspended in 150 millilitres of water, and this is poured into 300 millilitres of water which has just ceased boiling, and stirred well. The patient, in a fasting condition, eats the resulting gelatinous mass as soon as it has cooled sufficiently. Specimens of venous blood for sugar determination are taken before and thirty minutes, one hour, two hours and three hours after administration of the starch. If the starch solution is allowed to boil normal blood sugar curves may be obtained, so the preparation of the starch solution should be as mentioned. A glucose tolerance test after ingestion of 100 grammes of glucose should also be performed. The maximal rise in blood sugar content during the glucose and the starch tolerance tests is determined by subtracting the value for the fasting blood sugar of each curve from that of the peak of the respective curves. Then the extent to which the maximal rise in blood sugar content after glucose exceeds that after starch is calculated in percentage and compared with the normal range obtained from patients without diseases of the pancreas. Starch tolerance tests were performed on 27 control patients without pancreatic disease, approximately one-half of whom had diseases such as diabetes, chronic diarrhœa *et cetera*, which might theoretically interfere with the validity of the test. The test was also performed on 36 patients in whom pancreatic disease was diagnosed or suspected. The results of the test in the control group ranged from −54% to +51% with a mean of +13·9 and standard deviation of 28·2. The normal range is statistically calculated from these figures as −42·5 to +70·3, that is, mean ±2× standard deviation. Only the +70% is of importance. All results of the starch tests in the controls fell well below this. Of the 23 patients diagnosed as having chronic pancreatitis of one form or another, all but two gave figures well above the normal. Of the 10 patients suspected of having chronic pancreatitis, six gave a positive finding; the result was borderline in one and in the upper range of normality in another. The clinical diagnosis of the other two was doubtful; one gave a borderline test finding; in the other case the result was in the normal range. In a case of acute pancreatitis with latent diabetes the outcome of the starch tolerance test was borderline (+80%). Statistical analysis of the data shows that the difference between the control group and the group of patients with chronic pancreatic disease is highly significant with *P* (probability factor) = <0·01. The greatest use for this test will be in doubtful cases in which all the symptoms of pancreatitis are not clearly demonstrated.

[1] *Ann. Int. Med.*, September, 1954.

BLOOD LOSS DURING OPERATIONS ON THE NEWBORN.

AN important aspect of the welfare and management of newborn infants is brought out in a study reported by P. P. Rickham[1] on the blood loss sustained during operations on these infants. A consecutive series of 60 operations was studied. The blood loss was estimated by a colorimetric method, involving estimation of hæmoglobin in all blood collected on swabs and towels, and by a gravimetric method, in which weight comparison was made of swabs and towels before and after operation. It was concluded that the colorimetric method was the more satisfactory for the small amounts of blood usually lost in neonatal surgery. It was found that the pre-operative and post-operative hæmoglobin estimations on the child were of no value in estimating blood loss.

The blood loss during different operations varied considerably, even in operations for the same conditions and with the same technique. From this investigation and from previous experience with neonatal operations Rickham concludes that a blood loss of 20 to 25 millilitres can be ignored with two exceptions: first, in the small premature baby, especially those under four pounds in weight, in whom even small amounts of blood should be replaced; second, in operations for œsophageal atresia, which are often associated with extensive dissection in the mediastinum and considerable shock. He also found that the infants did well with a transfusion of 30 to 35 millilitres more than the amount of blood lost and believes that this slight over-transfusion is one of the reasons for the lowered operative mortality in his unit. If at the end of an operation when the blood loss is estimated it is found that the loss is greater than the amount that has been transfused, the baby is not removed from the operation table until the blood loss has been made good. Rickham stresses the fact that many of the extensive operations now performed on newborn babies are accompanied by considerable blood loss. Consideration might well be given to

[1] *Arch. Dis. Childhood*, August, 1954.

his recommendation that no operation should be commenced without having running an intravenous infusion, which can be changed over to blood at a moment's notice.

LOW PROTEIN DIETS.

THERE are still doubts as to what is the optimal daily consumption of protein, what is the minimum consumption over long periods compatible with health, and whether or not animal protein is an essential constituent of human diets. Recent papers throw some light on these questions. J. F. de Wijn, W. F. Donath and H. C. van der Meulen-van Eysbergen[1] describe a group of 60 subjects who had consumed no animal food for periods ranging from two to fifteen years previous to investigation (vegans). It is not stated whether they were male or female, nor are any details given of the nature and quantity of the food consumed. The diet was low in Calories and appreciably low in protein, calcium and riboflavin. Excessive intakes of provitamin *A*, nicotinic acid, vitamin *C* and iron were noted. Except for symptoms which could be ascribed to minor degrees of malnutrition in nine of the sixty subjects, they were all in good health and performed full employment in various jobs. Some had a mild degree of macrocytic anæmia. There was considerable underweight when they were compared with controls, the basal metabolic rate was high, and the pulse rate, blood pressure and pulse pressure were higher than those of controls on normal diet. Investigation of serum chemistry revealed no evidence of deficiency. The study revealed that the human organism has remarkable power to become adapted to various nutritive conditions, especially relatively low protein intakes with little or no animal protein.

Another study, by L. Mirone,[2] deals with a self-supporting community living on a diet low in protein content and devoid of meat. The individuals of this group had lived on this diet for twelve to forty-seven years doing all the hard work of a farming community, growing and preparing almost all their own food. Meat was never served. The only animal protein was skim milk in the bread and coffee, and a little egg a few times a year in raisin bread and cake. The total animal protein intake was 10 to 23 grammes daily. The people were very healthy, and the blood chemistry was normal in all respects. Clearly a diet free from meat and low in animal protein content is compatible with good health even though the total protein provided only about 10% of the total Calories.

P. György[3] has summarized recent work on the effects in man of diets very low in protein content. Protein malnutrition is a world-wide problem involving chiefly millions of people in the tropical belt of the world. Here it is seen predominantly in infants and children up to six or seven years of age. This type of protein malnutrition has been given the name "kwashiorkor" and has been described in detail in this journal during the past few months. A similar condition in Europe has been known as "starchy food dystrophy" and "*Mehlnährschaden*". This has recently assumed very great importance in Italy. A Nutritional Conference of the World Health Organization and the Food and Agricultural Organization of the United Nations held in Gambia in 1952 laid down the following rules:

> If the relative proportion of calories supplied by protein reaches a level of 15 to 20 per centum of the total calories in the daily diet, the protein requirement is sufficiently covered. This figure is reached in cow's milk. When the percentage of total calories supplied by protein is from 10 to 15 per centum (especially if the protein is of vegetable origin) the resistance of the organism is lowered. This is seen especially in cases of chronic infections. A ratio below ten per centum represents definite danger usually with symptoms.

The only obvious exception to this rule is, strangely enough, human milk, in which the ratio is only 6% to 7%. However, human milk has been found to be the best food and insurance against kwashiorkor and related conditions. The amino acid composition of human milk protein and its digestibility do not explain this superiority. György describes an N-containing polysaccharide obtained from human milk, and also from hog mucin, which he calls the bifidus factor and which, when added to cow's milk diluted to resemble human milk, gave significant growth-promoting effects in rats. Similarly it increased the growth-promoting properties of peanut meal. The reason is not yet clear.

An outstanding effect of prolonged protein deficiency is liver disease. Cirrhosis of the liver is extremely common in tropical countries and very common in children. This cirrhosis is found concomitantly with general malnutrition, which is usually based on a low intake of protein, particularly of animal protein. Primary hepatoma has a high incidence in countries where protein malnutrition is widespread, and György suggests that this is due to a combination of protein deficiency and some simultaneous "hepatoxic" constituent present in the diet.

In view of the large amount of work which has been done on the utilization of yeast as a cheap source of protein, it is of interest that a diet in which the sole source of protein is yeast produces very extensive liver necrosis in rats, and this is prevented by administration of vitamin *E* or the sulphur-containing amino acids. It is also considerably delayed by "Aureomycin", penicillin and "Terramycin", apparently through their effect on intestinal bacteria. Bacteria, however, are not essential ætiological factors in the development of liver necrosis, for the necrosis occurs in animals maintained germ-free from birth, although its appearance is much delayed. Apparently intestinal bacteria use up protective constituents of the food ingested and in consequence reduce their supply to the body. Intestinal bacteria then have to be taken into account in considering the amounts of different proteins needed to prevent protein malnutrition.

[1] *Proc. Nutrition Soc.*, 1954, Vol. XIII, No. 2.
[2] *Am. J. Clin. Nutrition*, July-August, 1954.
[3] *Am. J. Clin. Nutrition*, July-August, 1954.

AMPOULES.

THE Standards Association of Australia announces the issue for public critical review, as Document 284, of a draft Australian standard specification for ampoules. At the thirtieth session of the Australian and New Zealand Association for the Advancement of Science discussions on "ampouling" led to a recommendation to the Standards Association that a standard for glass ampoules be prepared. It was pointed out that variations in the thickness of glass and apertures of the stem cause great difficulty, in particular when automatic or semi-automatic filling or sealing equipment is used. Such equipment is now widely used, even for comparatively small scale "ampouling", and it is important that ampoules be as uniform in dimensions as possible. Inquiries by the Standards Association of Australia revealed wide support for the proposed standards and indicated that the latest British standard, 795:1953, Ampoules, would be largely suitable. The subcommittee appointed to consider the matter has now recommended endorsement of 795 subject to a few amendments, notably the addition of seven-millilitre and eleven-millilitre ampoules as used by Commonwealth Serum Laboratories. Copies of Document 284, which sets out the amendments, may be obtained from the headquarters of the Association, Science House, Gloucester Street, Sydney, and from branch offices in other capital cities and at Newcastle. The British Standard 795 may be examined at or purchased from these offices. The Association will welcome constructive comment from persons concerned with glass ampoules; such comment should be forwarded not later than February 16 1955.

Abstracts from Medical Literature.

PATHOLOGY.

Ductal Changes in Chronic Pancreatitis.

JAMES J. BERENS, ARCHIE H. BAGGENSTOSS AND HOWARD K. GRAY (*Arch. Surg.*, June, 1954) studied specimens of pancreas obtained at necropsy in 16 cases of chronic pancreatitis, with particular reference to the presence or absence of ductal dilatation. The duct of Wirsung was found to be grossly dilated in the tail of the pancreas in seven cases. In four other cases, histological evidence of dilatation of small ducts and ductules was present; focal inflammatory foci or ductal metaplasia may have been responsible. The relationship of ductal obstruction to the cause and progression of chronic pancreatitis is discussed.

Apocrine Adenoma of the Anus.

H. A. TELOH (*Cancer*, March, 1954) presents four examples of adenoma of the anus of apocrine-gland origin. He states that these tumours are basically benign neoplasms, do not invade or metastasize, and apparently do not recur. Their origin from apocrine elements is evidenced by the presence of a papillary structure, epithelial cells with a dome-shaped free edge, myo-epithelial elements and eosinophilic epithelial cells similar to those found characteristically in fibrocystic disease of the breast. The presence of holocrine elements suggests a common origin of apocrine and sebaceous tumours.

Primary Tumours of the Heart in Infancy and Early Childhood.

NOLTON H. BIGELOW, SIEGFRIED KLINGER AND ARTHUR W. WRIGHT (*Cancer*, May, 1954) report that, although primary tumours of the heart are rare, a surprisingly large number of some types are congenital or appear early in life, so that the term "congenital" is sometimes used in describing them. Other cardiac tumours occur no more frequently in very young individuals than could be explained by random or chance distribution. The morphological features of many are so unique and unequivocal that ready recognition of them is possible, although the interpretation and evaluation of almost all cardiac neoplasms are still unsettled. Two groups often indiscriminately called rhabdomyomata are considered. One group, designated as primitive fibromata or rhabdomyofibromata, is characteristic. These tumours are not so rare as commonly believed, because they have been classified by such a welter of diagnostic terms that their probable identity as a specific type of neoplasm has not previously been clearly recognized. Another group, also called by a variety of terms, is considered to be a non-neoplastic form of nodular growth best characterized as an instance of congenital rhabdomyomatosis. Reports of primary malignant tumours in infancy and early childhood are uncommon, but, of the few cases reported, only one, that of a malignant teratoma, is considered fully acceptable, while one case of fibrosarcoma may possibly have originated in the heart. Two cases are reported of cardiac tumours illustrative of two different types of growth that often appear in early infancy.

Œstrogenic Ovarian Tumours.

R. W. BURSLEM, F. A. LANGLEY AND A. S. WOODCOCK (*Cancer*, May, 1954) review 25 granulosa-cell tumours, two tubular androblastomata and 40 thecoma-fibromata on a clinical and histopathological basis. They state that clinically evidence of œstrogenic activity, shown by precocious puberty, menstrual disturbance or post-menopausal bleeding, is found to be of most diagnostic value. It occurred in 18 of the patients with granulosa-cell tumours and in 20 of those with thecoma-fibromata. There are no other symptoms distinct from those produced by ovarian tumours in general. Seven granulosa-cell tumours in the series were malignant; of these six occurred in patients after the menopause. None of the tumours in the thecoma-fibromata group was malignant. Before the menopause, therefore, oophorectomy appears adequate surgical treatment, but in post-menopausal patients panhysterectomy with bilateral salpingo-oophorectomy is indicated. A careful follow-up is necessary, for recurrence was noted in this series as long as eight years post-operatively. Histologically a description is given of the three types of tumour—granulosa-cell tumour, tubular androblastoma and thecoma-fibroma. The features by which previous writers have attempted to differentiate between thecoma and fibroma are analysed, and it is shown that, in general, a clear-cut distinction between thecoma and fibroma is not possible. The histogenesis of the three groups is discussed. Their related features are explained on their common origin from the cœlomic mesenchyme. Their maximum incidence about the menopause supports the suggestion that increased output of pituitary gonadotrophin stimulates latent competences in the ovary to tumour production. Experimental tumorigenesis in animals is quoted as further evidence for this theory. Doubt is expressed as to the truly neoplastic nature of some of these tumours, and it is considered that many are hyperplastic rather than neoplastic.

Mucinous Cystadenomata and Mucinous Cystadenocarcinomata of the Ovary.

MILDRED CARIKER AND MALCOLM DOCKERTY (*Cancer*, March, 1954) found that in a series of 355 cases of ovarian mucinous tumours histogenetic evidence favoured teratomatous origin. Dermoids were associated in 4·5% of the tumours. The intestinal enzymes diastase, lipase, trypase, trypsin, amylase and sucrase were found in three specimens of fresh cystic fluid. Microscopically, the lining epithelium of the cysts was like that of entodermal-derived structures of the gastro-intestinal tract. Contrary to expectations Brenner tumour was found in only two cysts. A relationship between serous and mucinous cysts was suggested by the finding of 45 cases (not included in this series) in which the patient was reported to have had microscopic characteristics of both. Malignant growths were present in 38·9% of cases; 76·8% of the total number of malignant lesions were cystadenocarcinomata, Grade I. The five-year-survival rate of this group was 69·7%. None of the four patients having a lesion of Grade III was known to have survived. There were no lesions of Grade IV. Both benign and malignant epithelium may be found in the same tumour, necessitating the study of multiple samples and sections of each tumour. The knowledge of the presence of malignant changes is most important to the surgeon, so that all ovarian tissue may be removed, the possibility of recurrence being thereby diminished. It is thought that malignant tumours probably arise from the originally benign neoplasms in ovarian mucinous tumours. A characteristic papillary arrangement of epithelial-cyst lining can exist in a benign tumour, but as a blunt, scantily branching type of projection. The diagnosis of benignancy or malignancy rests primarily on the cytological findings. If the tumour is malignant, all ovarian tissue should be removed at the time of the initial operation. The second ovary should also be removed regardless of the person's age and even though the tumour is benign if there is evidence of cystic formation. The cysts tend to become large, and this fact makes spontaneous rupture a possibility. Contact of the contents of a malignant cyst with the peritoneum predisposes to the development of *myxoma peritonæi*. This insidious complication is responsible, through slow intestinal obstruction, for the greatest number of deaths among patients having mucinous cystadenomata or mucinous cystadenocarcinomata of the ovary and is little affected by any treatment. In contrast, the accidental rupture of a malignant mucinous cyst in removal or its evacuation before removal apparently does not affect the prognosis adversely.

Hürthle-Cell Tumours of the Thyroid.

ROBERT C. HORN (*Cancer*, March, 1954) has reviewed the clinical data and pathological material of 75 cases of circumscribed thyroid nodules composed principally or wholly of Hürthle cells. In 14 cases the lesions have been classified as involutional nodules, in 27 as adenomata and in 34 as carcinomata. The carcinomata composed of Hürthle cells may be readily segregated according to the classification used for thyroid tumours in which Hürthle cells do not form a conspicuous component. The degree of clinical malignancy displayed by these various tumour types corresponds to that of the various usual types of thyroid carcinoma. In 12 of the 34 cases of carcinoma, the diagnosis of malignancy rests upon morphological appearance alone. In the remaining 22 it is supported by a malignant clinical course or by the demonstration of invasive growth. Of the 22 proved carcinomata, five are classified as malignant adenomata, five as follicular, four as papillary, four as adenocarcinomata, and four as giant and spindle cell tumours. This material supports the contention that the so-called Hürthle-cell tumour is not a specific tumour type,

but that Hürthle cells may occur, even to the point of virtual exclusion of other cell types, in any thyroid lesion. Thus, Hürthle-cell lesions may be non-neoplastic, benign tumours or carcinomata of any degree of malignancy. Emphasis is placed on the frequency with which Hürthle cells are pleomorphic and on the fact that pleomorphism is frequently of no diagnostic significance.

Pigmented Nævi, Juvenile Melanomata and Malignant Melanomata in Children.

HENRY E. MCWHORTER AND LEWIS B. WOOLNER (*Cancer*, May, 1954) have made a study at the Mayo Clinic of 172 surgically removed pigmented tumours of children. Analysis revealed 149 pigmented nævi, seven blue nævi, 11 juvenile melanomata and five malignant melanomata. The benign pigmented nævi were found to have histological characteristics similar to such lesions in adults, except that they tend to portray more actively growing earlier stages in the evolution of the nævus. Because a few lesions may show this quality of proliferation to a great extent, they have been mistaken for malignant melanomata. Clinically and histologically, the 11 juvenile melanomata appear to be specific benign lesions that can be differentiated from malignant melanomata, for which they often have been mistaken in the past. Death occurred in four of the five cases of malignant melanoma in children. A survey of the literature revealed at least 13 additional authentic cases of malignant melanomata in children. True malignant melanomata in children are rare lesions. It remains to be proved that such lesions differ either clinically or histologically from malignant melanomata in adults.

MORPHOLOGY.

The Human Embryonic Heart.

R. H. LICATA (*Am. J. Anat.*, January, 1954) states that although present knowledge of the development of the heart is extensive, there are many phases which require reexamination. The present study was undertaken to ascertain the state of development of certain rapidly changing structures at relatively advanced stages which, as yet, have not been studied in detail. This study in the ninth week of development was based primarily on wax-plate reconstructions augmented by transparent plastic reconstructions of certain regions and microdissections of ninth-week embryos. This stage was selected because most of the cardiac structures recognized in the adult are already clearly established and yet are still sufficiently embryonic to reflect the developmental processes involved in their origin. The interatrial septal complex is of particular interest. There has been extensive resorption of *septum primum* to form a large *ostium secundum*. A thick, but not yet fully developed, *septum secundum* delimits a wide *foramen ovale*. This arrangement leaves a much freer interatrial communication than is characteristic of the heart at term. The right venous valve is extraordinarily highly developed at this age, whereas the left venous valve already has been considerably reduced. As a result there is a deep sinal bay of the right atrium between the right venous valve and the interatrial septal complex into which all the major veins empty. The morphology of this region suggests that a considerable part of the inferior caval blood-stream passes directly through the interatrial "functional orifice" into the left atrium. The right venous valve may well act as a baffle helping to insure adequate charging of the left atrium, which still has only a relatively small direct return from the lungs. In the sinal bay there must be considerable mixing of the blood entering by way of the superior *vena cava* and the coronary sinus with that part of the inferior caval blood that does not go to the left atrium. By the ninth week all the major cardiac vessels are present and there are already special branches to the sino-atrial node and to the main atrio-ventricular bundle. Both divisions of the autonomic supply are represented in the ninth-week heart, but the parasympathetic branches from the vagus are more highly developed than the sympathetic branches. Local aggregations of neuroblasts are found in many areas in relation to the heart and the great vessels. A well-defined primordium of the sino-atrial node can be identified by the ninth week. The bundle of His, with its major branches, is the most strongly developed component of the conduction system at this age. The atrio-ventricular node was not clearly recognizable and the terminal (Purkinje) fibres were as yet undifferentiated from the rest of the cardiac muscle fibres.

Age Changes in Human Head Hair.

O. H. DUGGINS (*Am. J. Phys. Anthropol.*, March, 1954) presents the results of a study of refractive indices of the cuticle of hair from 16 white subjects from birth to the age of twenty years. Differences and similarities between sexes or individuals of the same sex were studied and age changes noted. The refractive indices of the cuticle of hair fluctuate greatly during the first two years of life, and between the ages of three and seven years the indices of boys and girls approximate each other rather closely with no evidence of divergence according to sex. From eight to sixteen years there is a sharp drop in refractive indices of the hair of girls, and their indices fall well below the levels for those of boys. After sixteen years the indices approach each other again, the level in girls being slightly lower than that in boys. The author states that refractive indices of hair may be of value in indicating the approximate age and sex of the individual.

Ocular Parasympathetic Nerve Supply.

R. WARWICK (*J. Anat.*, January, 1954) reviews the extensive literature concerning the ocular parasympathetic nerve supply and states that, although convincing evidence exists that this pathway issues in the oculomotor nerve and relays in the ciliary ganglion, its mesencephalic sources, reputedly the Edinger-Westphal nuclei, are less satisfactorily substantiated. The retrograde response to interruption at numerous points in this pathway was therefore studied in cats and particularly in monkeys; the latter have seldom been used in investigating this problem. All lesions affecting the short ciliary nerves (for example, enucleation, exenteration, ciliary neurectomy) produced chromatolysis in about 97% of the cells of the ciliary ganglion. After iridectomy about 3% only of these cells showed such changes. These results confirmed the view that practically all the cells in the ciliary ganglion innervate intrinsic ocular musculature; they also showed that a small fraction only of their axons supply the *sphincter pupillæ*. Ciliary ganglionectomy and division of the third nerve (in monkeys) regularly caused a retrograde reaction of striking degree in most of the cells of the ipsilateral Edinger-Westphal nucleus and in the ipsilateral half of the antero-median nucleus. Topographical observation showed that these nuclei form a continuous small-celled mass in the macaque. It must be concluded that the usual account of the Edinger-Westphal nucleus as the parasympathetic component of the oculomotor complex is correct, and that the antero-medial nucleus is an integral part of this centre.

Structure and Function of Fibrocartilages within Vertebrate Joints.

C. H. BARNETT (*J. Anat.*, July, 1954) dissected sixty joints containing fibrocartilages in various species of vertebrates, and paid particular retention to the type of movement occurring at such joints. He found that intraarticular fibrocartilages are reinforced by bony lunulæ if they are steeply wedged in transverse section. Fibrocartilages usually occur in those articulations in which flexion and extension are associated with gliding, a combination of movements that demands a well-rounded entering surface and a relatively flattened receiving surface. The interposition of a fibrocartilage, the mobility of which is under ligamentous or muscular control, helps to prevent instability of the joint. In bicondylar joints, gliding movement is usually necessitated by axial rotation. Where axial rotation occurs without gliding, as in the medial half of the knee of the tortoise, no fibrocartilage is present. In some joints, notably the temporomandibular joint of carnivores, fibrocartilages may reduce the likelihood of attrition of the receiving articular surface by ensuring that a constantly changing region bears the pressure of the entering surface. Fibrocartilages may also perform the functions of increasing the range of movement at a joint and acting as thrust-pads.

Development of the Human Femur.

WILLIAM J. L. FELTS (*Am. J. Anat.*, January, 1954) reports a very full investigation on the manner of growth and development *in toto* of the prenatal femur. Such a comprehensive study on a prenatal long bone has never before been made. The material examined consisted of 53 femurs, from 53 fœtuses and neo-natal infants.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal Alexandra Hospital for Children, Camperdown, New South Wales, on June 17, 1954. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staffs of the hospital. Part of this report appeared in the issues of November 13 and 27 and December 4, 1954.

Neuroblastoma.

DR. D. H. COHEN showed a boy, who had been first examined in December, 1953, with a mass of large glands in the right inguinal region. The mother stated that the glands had been present for about six months and had been slowly increasing in size. On examination of the patient, the glands were discrete, very hard and not tender. Clinically they appeared to be obviously neoplastic, and Hodgkin's disease was considered the most likely diagnosis. Examination of the blood revealed no abnormality, and an X-ray film of the chest was clear. Clinical examination revealed no other abnormality. No other gland groups were involved and the spleen was not palpable. In view of the local nature of the condition, radical removal of the inguinal, femoral and deep iliac glands was undertaken in December, 1953, all obviously enlarged glands being removed as far as the common iliac vessels. Apart from a serous effusion which required aspiration, convalescence was uncomplicated and a course of deep X-ray therapy was commenced. Pathological examination of the removed glands revealed the growth to be a neuroblastoma, presumably secondary. However, a careful search failed to reveal any definite evidence of a primary focus. The only suggestive finding was a small area of calcification above the right kidney; but perirenal pneumography showed the right adrenal to be of normal size. However, in view of this, the right adrenal was included in the area of irradiation. Dr. Cohen said that the child had continued in good health since operation, and so far there was no evidence of any recurrence.

Hodgkin's Disease.

Dr. Cohen's next patient was a boy, who had first presented with enlargement of the right cervical glands of twelve months' duration. The glands had become progressively larger during that time, and no other groups were affected. On examination of the child, the jugular chain of glands on the right side of the neck was seen to be very considerably enlarged. The glands were discrete, non-tender and rubbery in consistency. The general health was good and no other abnormality was discovered on clinical examination. The spleen was not palpable, and no other gland groups appeared to be involved. Examination of the blood disclosed a mild hypochromic anæmia, but no other abnormality. An X-ray film of the chest revealed no abnormality. The character of the glandular enlargement suggested a neoplastic basis, and Hodgkin's disease was considered the most likely diagnosis. In view of the extremely localized nature of the condition and the absence of any evidence of more distant spread, it was decided to perform a radical gland dissection on the right side of the neck. This was done on November 2, 1953. The internal jugular vein and sterno-mastoid were preserved, but all the superficial and deep lymph glands in the region were removed. Post-operatively, deep X-ray therapy was commenced. Dr. Cohen said that there had been no evidence of any recurrnece so far, and, although it was far too early to be hopeful of a cure, the boy's progress to date was encouraging.

Rhabdomyosarcoma of Calf Muscles.

Dr. Cohen finally discussed the case of a girl who had been referred from the country, where a mass had been excised from the muscles of the right calf in September, 1953. The report of the pathologist was "hæmangioendothelioma". When the girl was first examined, there was a recent scar on the posterior aspect of the right calf with some thickening under it, which suggested incomplete removal. In view of the pathological report she was sent back, with an encouraging prognosis and a request that she be referred again if the mass grew rapidly. She was sent down again in December, with a mass in the right calf of considerable size, which was obviously infiltrating the muscles of the leg. In view of the rapid increase in size of the tumour, she was immediately admitted to hospital. Examination of frozen sections of a biopsy specimen revealed a highly cellular tumour of high malignancy, and a supracondylar amputation was performed. Subsequent pathological examination showed the growth to be an extremely undifferentiated rhabdomyosarcoma. The original slides were obtained from the Board of Health, and the character of the original growth was seen to be identical with the recurrence. Unfortunately, wide dissemination rapidly occurred, and evidence of metastasis in the mandible appeared while the child was still in hospital, after which she rapidly went downhill.

Congenital Deformities of the Tibiæ.

DR. L. MACDONALD showed a child, aged thirteen years, who had first been examined on February 4, 1940, at the age of five weeks. The child was the first in the family, and the birth was normal. Bilateral tibial deformities had been noticed at birth. X-ray examination revealed irregular destruction of the lower end of the tibia. The markings of the lesion were smooth, and some areas of the cortex were destroyed. Neither the Wassermann nor the Kahn test result was positive. In 1948, gradual improvement in the line of the tibia took place over a period of nine months; night splints and leg moulding were used during that period. X-ray examination showed that the bone structure was much improved, but considerable anterior bowing was still present. Cystic change was seen in the upper third of the tibia. In 1949, an X-ray examination of the lower third of the tibial shafts still showed considerable bowing, but the bone structure was good. The cystic area in the upper part of the tibia was diminished, but some destruction of bone was seen on the medial cortex. In March, 1950, an X-ray examination revealed no cystic areas remaining in the right tibia. The clinical alignment was improving. In October, 1950, an X-ray examination still revealed fairly pronounced anterior and lateral bowing of the middle and lower third of the right tibia. No cystic change was seen at the site of the bowing. A well-defined small cystic area had appeared at the junction of middle and upper thirds of the tibia; that cyst resolved in eight months. In November, 1953, an X-ray examination revealed no cystic areas, and slight forward and outward bowing.

Developmental Abnormality of Tibia and Fibula.

Dr. Macdonald's second patient had presented on February 16, 1949, at the age of seven months, with bowing of the left tibia. X-ray examination revealed pronounced lateral bowing at the junction of the middle and distal thirds of the left tibia, with narrowing of the bone at that site. The condition was thought to be developmental in origin, and a similar condition was present in the fibula; it was probably allied to pseudoarthrosis. On November 17, 1949, some clinical improvement had occurred, and the patient, then aged sixteen months, was beginning to walk alone. The X-ray appearance suggested that fractures, possibly intra-uterine or birth fractures, of the left tibia and fibula had occurred. The bones were somewhat attenuated in the region of the lesion, which suggested that the condition was probably an intrauterine fracture without the formation of a pseudoarthrosis. The fractures had united solidly with lateral bowing.

On June 14, 1950, an X-ray examination revealed a fracture through the site of the previous lesion. The leg was put in a plaster cast. By December 13 no union had occurred. In the following two-year period, little union occurred and a pseudoarthrosis developed. On October 21, 1953, the pseudoarthrosis was removed, and a sliding bone graft from the proximal fragment of the tibia was inserted. On March 17, 1954, the graft had become incorporated in the upper and lower fragments, but had fractured at the site of the pseudoarthrosis. On May 26 good alignment was present, with some clinical union at the fracture site. X-ray examination showed that the X-ray bone graft was firmly incorporated in the lower fragment, and there was insecure union of the upper fragment. There was some cupping of the upper and lower fragments, but little sclerosis.

Poliomyelitis with Muscle Transplant.

DR. R. L. STEPHEN showed a child, aged eleven years, who in January, 1953, had suffered from poliomyelitis affecting the right arm, especially the hand, and the left leg. Slow but steady improvement went on for several months. However, the right *opponens pollicis* and the short abductor of the thumb had no recovery. The left leg was left diffusely weak. On October 22, 1953, the tendon of the superficial flexor of the ring finger was transplanted to a drill hole in the proximal phalanx of the thumb; a plaster cast was applied with the hand in palmar flexion for a month. On February 8, 1954, a triple arthrodesis was performed on the left foot with removal of the navicular bone. At the time of the meeting, the tendon transplant of the right thumb

was seen to cause excellent opposition. The right foot was in a short leg walking plaster.

Poliomyelitis with Tendon Transplant.

Dr. Stephen's second patient was a child, aged twelve years, who in January, 1951, had suffered from poliomyelitis, with residual weakness of the right shoulder and hand especially affecting the *opponens pollicis* and the small muscles. On November 5, 1953, the *flexor digitorum sublimis* of the ring finger was inserted into the proximal phalanx of the thumb by the Bunnell technique, and on December 7 the plaster splint was removed. In March, 1954, there was good opposition of the thumb. Shoulder abduction was poor, but improving.

Poliomyelitis with Muscle Transplant.

Dr. Stephen next showed a child, aged nine years, who early in 1950 had suffered from poliomyelitis affecting the left arm, especially shoulder abduction and all movements of the elbow. The arm was kept on an abduction splint, and gradually the elbow improved, but shoulder abduction remained absent. Power in the trapezius was good, but that in the rhomboids was only fair. Arthrodesis of the shoulder was considered. On January 1, 1954, a strip of *fascia lata* was transferred from the trapezius to halfway down the humerus. At the time of the meeting, anti-gravity abduction of the left shoulder was present.

Slipped Epiphysis.

The next patient shown by Dr. Stephen was a girl, aged twelve years, who in June, 1953, fell and thereafter was unable to bend her left leg properly. Later she developed a limp and pain in the left knee on weight-bearing. She was put to bed for two months. X-ray examination revealed early slipping of the left femoral epiphysis, and she was admitted to hospital and traction was applied to her left leg for two months. On May 28, 1954, she was admitted to the Royal Alexandra Hospital for Children with a slipped upper femoral epiphysis. On examination, she was seen to be an obese adolescent girl. Her left hip was moderately adducted and externally rotated. Serial X-ray films showed progressive slipping of the upper femoral epiphysis from the earliest stage.

Diaphyseal Aclasis.

Dr. Stephen then showed a girl, aged ten years, who on March 8, 1954, complained that her right leg hurt, and that she fell over a lot. The right leg swelled grossly, but there was no history of injury. On examination of the patient, there were multiple exostoses near the joints, especially pronounced above the right ankle. There was lateral rotation of the right tibia, but no swelling and no palpable glands. X-ray examination revealed multiple exostoses of diaphyseal aclasis. On June 10 arteriography was performed.

Tuberculous Arthritis.

Dr. Stephen next showed a child, aged three years, who was examined on February 15, 1954, because of swelling of the right knee present for eighteen months. The child's father had died of tuberculosis seven months previously. On examination of the child, synovial thickening was present in the right knee. The Mantoux test produced a positive reaction with a dilution of one in 1000. X-ray examination of the knee revealed no abnormality. An X-ray examination of the chest revealed a focus of calcification in the left hilar region. The mother was reluctant to permit the child's admission to hospital. On February 19 the patient was admitted to hospital and immobilized, and treatment with streptomycin and PAS was commenced. On March 25 synovectomy was carried out on the right knee. Histological examination of the material removed revealed tuberculous granulation tissue. On May 19 there was no clinical or radiological evidence of tuberculosis except for areas of osteoporosis. The erythrocyte sedimentation rate was normal, and streptomycin treatment was suspended.

Tuberculous Arthritis.

Dr. Stephen finally showed a male child, aged five years, who had had a limp in the leg at the age of three years; the limp subsided in two or three weeks without treatment. Fourteen months later he complained of pain in the right hip. His brother had had a tuberculous gland removed three months beforehand.

The boy was admitted to the Royal Alexandra Hospital for Children on September 16, 1953. There were no abnormal physical signs except slight limitation of flexion. An X-ray film of the chest was clear. An X-ray examination of the hip revealed pronounced osteoporosis of the right femoral head epiphyses and of the acetabular margins; this suggested early tuberculosis. The erythrocyte sedimentation rate was 40 millimetres in one hour, and the Mantoux test produced a positive reaction with a dilution of one in 1000. On October 22 *débridement* of the left hip was carried out through a limited Smith-Petersen incision under streptomycin "cover". The histological findings were those of tuberculosis. On May 8, 1954, full painless movement was present, and on May 10 weight-bearing commenced. At the time of the meeting, the right hip appeared normal except for the small scar.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

INFLAMMATORY FEVER.[1]

[Executive Council Minute Number 42.]

October 9, 1838.

His Excellency the Governor laid before the Council a letter received yesterday from the Deputy Inspector General of Hospitals transmitting a letter addressed to him by John Reid Esq. Surgeon Superintendent of the ship William Rogers dated eight o'clock A.M. October the eighth informing him that sixteen of the Emigrants in that vessel were then confined to bed with Inflammatory Fever of which they had been taken ill since the ship was released from quarantine and requesting that they might be moved to the Hospital on shore: to which step the Deputy Inspector General expressed himself as strongly opposed, being apprehensive that if adopted, it might be the means of introducing that formidable disease into the hospital. His Excellency informed the Council that upon the receipt of the Communication above mentioned, he had directed a medical Board to proceed immediately alongside the William Rogers, and upon receipt of their Report, he had directed that vessel to return with as little delay as possible to Spring Cove and that the Emigrants should be immediately landed there: the sick being separated, and placed under the charge of Surgeon Reid: and further that the usual precautions should be taken with regard to fumigating and ventilating; it appearing from the report of the Medical Board above referred to, that the whole of the sixteen cases of fever have originated within the short period of 3 days and that four of the cases are very seriously dangerous, and that the Board are of opinion that the disease is now infectious, and that all the usual rules and precautions should be strictly observed.

Correspondence.

DEATHS ASSOCIATED WITH ANÆSTHESIA AND SURGERY.

SIR: In your issue of November 6, 1954, you publish a comment on an article entitled "Deaths Associated with Anæsthesia and Surgery" by H. K. Beecher and D. P. Todd.

This article, while provoking useful and critical discussion amongst anæsthetists, can do much harm by giving false impressions, in particular, about the dangers of relaxants. Beecher and Todd claim, from their figures, that there is a significant increase in anæsthetic death rate when muscle relaxants are employed. When major operations are compared, the death rate is six times higher in the curare group than in the non-curare group. They then proceed to try to show that relaxants, *per se*, were the cause for a high proportion of these cases, the mechanism of death being primary circulatory failure. They, however, give no details of these cases nor of the measures taken for resuscitation. The reader is assured that artificial respiration "of a generally effective type" has been applied. However, when we study their figures more closely, we find that the total number of cases receiving muscle relaxants is 44,100, while only 13,800 of all the cases under anæsthesia

[1] From the original in the Mitchell Library, Sydney.

had any form of assisted or controlled respiration—surely a tacit admission that the hazards of under-ventilation could well be a feature.

Another important aspect which does not get sufficient prominence in your review is the fact, already well known to anæsthetists, that the dangers of combination of a relaxant with ether or cyclopropane are considerably greater than the use of thiopentone, nitrous oxide and a relaxant. It would be a great pity if the combination of thiopentone, relaxant and nitrous oxide, which has proved so safe and satisfactory in the hands of skilled anæsthetists, should be discredited.

This article, which is receiving wide publication and acceptance, may show trends in the United States of America, but does not reflect the common practice which rules among properly qualified specialist anæsthetists in Australia today.

Yours, etc.,

Melbourne, PATRICIA WILSON, D.A., F.F.A.R.C.S.
November 16, 1954.

CONCERNING PROCTOLOGY.

SIR: This discussion is getting somewhat muddled. Dr. Fowles states that I follow conventional methods which over the years have given no thought to the surgical aftermath of pain and stricture, which occurs all too often in operations in this area. But these so-called conventional methods have been evolved in great proctological centres to eliminate the strictures so common after the Whitehead and similar operations, and also the pain and recurrent abscesses of sewing operations. Dr. Fowles praises Dr. Starr for trying to stop strictures and pain by using methods calculated to cause them, and mentions me as causing strictures and pain by using methods evolved to prevent them. But I admit it must be difficult to observe proctological techniques from the head of the table.

If Dr. Fowles is ever in London, I suggest he go to the Gordon or St. Mark's Hospital and ask to see some post-operative strictures. His reception would be similar to that of the hapless student who once asked a ward sister to show him some bed sores.

Incidentally, in case Dr. Starr's absence from these discussions should be wondered at, I feel it should be stated in all fairness that he left for the United States of America shortly after his original letter appeared. Doubtless, on his return, we shall hear more from him. If he offers valuable additions to our knowledge, I shall agree with Dr. Fowles—good luck to him!

Yours, etc.,

149 Macquarie Street, C. H. WICKHAM LAWES.
Sydney,
November 17, 1954.

UNILATERAL BRACHIAL PARALYSIS AFTER ANÆSTHESIA WITH THIOPENTONE, "FLAXEDIL" AND NITROUS OXIDE.

SIR: There is food for thought in the formidable list of five cases of post-anæsthetic brachial plexus paralysis reported by Dr. Winifred Wall, of Adelaide (M. J. AUSTRALIA, October 23, 1954). Four different types of abduction of the arm are involved: deep Trendelenburg, Millin's prostatectomy, gastrectomy and crucifix position for simple mastectomy. With increased use of veins for relaxants and therapy, and the need for blood pressure readings during operation, the mechanism of such an injury is worthy of a lot of attention.

The patient does not have to be overweight. My own case was of medium build, exsanguinated to 30% hæmoglobin, restored pre-operatively to 80% with other people's corpuscles. Her arm was abducted and supinated to palm uppermost for blood pressure recordings at the cubital fossa during a long hysterectomy. Recovery from the brachial palsy took nine months.

It could be that the biggest single factor causing overstretching of the cords of the brachial plexus in such positions is the bulging into their path of the articulating head of the humerus. This can be demonstrated with a matching scapula and humerus and a little experimentation, lying recumbent like the patient. With the left arm at the side and the forearm flexed across the chest the medial epicondyle of the humerus is at seven o'clock. On abducting the straight arm to 90° the medial epicondyle rotates anticlockwise to four o'clock (45°). On full supination further movement occurs to three o'clock (60°). Transferring this movement to glenoid fossa and head of humerus it is seen that not only has the shaft of the humerus been carried an inch away from the anterior run of the glenoid fossa, but the rounded head has rotated into the path of the plexus. In the patient only the subscapularis muscle lies between the head and the nerves.

Anyone caring to check this before getting up in the morning will probably be surprised at the way the head of the humerus bulges forward on such abduction. Such a theory fits in with the fact that muscles supplied by the posterior cord—axillary (circumflex) and radial nerves—suffer most and are last to recover. The nerves are anchored in the rotated muscles and are stretched over the head of the humerus. Further down the shaft of the humerus the radial nerve is anchored in the groove round the bone. So wrist drop is severe and long. In the Millin's prostatectomy case, wrist drop was the only injury, so it probably occurs first. In any event, whatever causative theory is correct, one thing is clear—abduction of the arm to 90° with the use of relaxants is hazardous in long operations with the head of the table below horizontal. Supination in extension increases the hazard; flexion of the elbow reduces it. Abduction to 45° appears to be the limit of safety. It seems necessary for someone to design an operating table fitting incorporating these points.

Some such thing as a two-tier fitting, the lower plate supporting the humerus at 45° abduction, a rest above for the forearm flexed back so that the palm lies above and faces the shoulder joint.

Yours, etc.,

Williamstown, LEO J. GURRY.
Victoria,
November 15, 1954.

THE COLLEGE OF GENERAL PRACTITIONERS: QUEENSLAND FACULTY.

SIR: In reply to Dr. B. J. Bouché and his remarks concerning the College of General Practitioners, I would call his attention to the aims of the College. The main aim is to raise the standard of general practice and hence the prestige of general practice throughout the State—not just to perpetuate the standard as required by law. It has never been suggested that a bachelor's degree in medicine and surgery will automatically ensure admission to a College of Physicians or Surgeons.

With regard to item (c) of Dr. Adsett's letter, the College Board is firmly of the opinion that post-graduate study is desirable for everybody. This condition can be waived in those senior practitioners who have had twenty years' experience of active practice and who are otherwise eligible. It will be quite easy to meet members of the College during post-graduate courses and make, we hope, such a favourable impression that nomination is assured.

Dr. Bouché's expressed opinion that the only criterion for membership should be that the applicant is in general practice and has not been struck off the register, would defeat the aims of the College. There is already the British Medical Association, which exercises these criteria. Membership of the College will imply some further evidence of a desire to raise the standard of general practice by undergraduate or post-graduate teaching or by research in general practice.

Yours, etc.,

PAUL HOPKINS,
Warden, Queensland Faculty,
College of General
Practitioners.

Mackay,
Queensland,
November 18, 1954.

INDUCTION OF LABOUR.

SIR: Dr. B. J. Bouché, of Boulia, Queensland, asks for guidance from my department on the subject of induction of labour (M. J. AUSTRALIA, November 6), his difficulties having been provoked by Dr. F. A. Bellingham's recent survey of the subject (M. J. AUSTRALIA, October 2).

The various techniques for the induction of labour that have been developed over the years may appear confusing, but have at least one common objective—that of striving for the most physiologically sound and effective method (if such exists). If I were to attempt to meet Dr. Bouché's wishes by a series of short dogmatic statements, these (however unsatisfactory) would be along the following lines.

There is still no really effective method of induction of labour that will suit all cases. The medicinal induction of labour is (or should be) used less frequently, and repeated medicinal inductions are out of favour. Quinine has been dropped as a sensitizing agent, and œstrogens are only useful following intrauterine death and retention of the fœtus, and in association with uterine hypotonus. Oxytocics are being used in much smaller doses than previously, and prior "stripping of membranes" is often a useful adjunct.

"Tubal" induction of labour is condemned by many and lauded by some. I would be sorry to see it discarded altogether—with proper technique and precautions it is often a useful alternative to the "Pitocin" drip (q.v.) and to surgical delivery in those patients with a closed cervix.

I do not share Dr. Bouché's horror at Dr. Bellingham's attempts to produce a "ripe" cervix for artificial rupture of the membranes by prior medicinal stimulation. However, as Dr. Bellingham would probably agree, it will only be successful in a proportion of cases, and the time factor involved may well demand some alternative procedure.

Artificial rupture of either the forewaters or hindwaters remains the most generally useful method of induction, but the reasons for apparent failure in some cases should be carefully studied. Briefly, the ideal case is one in which, other desiderata having been met, the cervix is neither too "ripe" nor too "unripe". The latter condition is well known, but the former is one which is not always recognized; the cervix is extremely patulous, and the membranes can be stripped from the lower segment and ruptured with the greatest of ease, but labour does not ensue. The condition is due to uterine hypotonus, and the ideal treatment is the administration of a "Pitocin" drip. Alternatively, œstrogens followed by repeated injections of small doses of oxytocin will often lead to success.

The "Pitocin" drip technique requires constant and skilled supervision, but is becoming increasingly availed of in teaching hospitals where the supervision can be at registrar level. It offers an almost physiological and an effective alternative to tubal induction and to Cæsarean section or hysterotomy in those patients in whom the indication is an urgent one, the cervix is firmly closed and there is no cephalo-pelvic disproportion or malpresentation. It is not a technique suited to private obstetric practice.

The foregoing remarks are purposely of a general nature. However, Dr. Bouché has raised the question of induction of premature labour for potential erythroblastosis. May I suggest that even more important than when to induce labour is the matter of where to induce labour. Because of the tremendous advantages of exchange transfusion for such infants and the highly technical nature of the procedure, the correct treatment would now appear to be the transfer of the mother at approximately thirty-seven weeks' gestation to a centre where exchange transfusion and specialized nursing and after-care of the infant can be carried out. Under these circumstances the exact timing of the induction becomes less important.

Yours, etc.,

Department of Obstetrics, The University of Queensland, Brisbane.
G. SHEDDEN ADAM.

November 16, 1954.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Conferences on Post-Graduate Medical Education.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that the second conference on medical education on "The Training of Specialists", will be held on Wednesday, March 2, 1955, and the third conference on "Post-Graduate Education of the Practising

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED NOVEMBER 13, 1954.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Aust. tls.
Acute Rheumatism	2	1(1)	11(8)	..	..	..	..	..	14
Amœbiasis	..	..	..	1(1)	..	..	..	..	1
Ancylostomiasis	1(1)	..	..	..	..	..	..	..	1
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	10(6)	5(3)	14(9)	..	..	..	..	6	35
Diphtheria	..	2(2)	3(2)	..	3(3)	..	..	..	8
Dysentery (Bacillary)	..	..	..	..	..	..	..	..	..
Encephalitis	1(1)	1	..	..	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	1	..	..	..	..	..	..	1
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	80(40)	66(47)	..	..	1(1)	..	..	2	149
Lead Poisoning	..	..	..	..	3	..	..	..	3
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	2	..	..	..	..	..	2
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(1)	1(1)	..	1(1)	1(1)	..	..	..	5
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	1	..	..	..	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	5(3)	7(2)	2(2)	4(1)	3	..	..	..	21
Puerperal Fever	1(1)	..	..	..	..	..	..	..	1
Rubella	..	27(24)	..	..	15(15)	..	..	..	42
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	38(9)	20(9)	6(3)	4(4)	..	..	..	..	68
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1	..	..	..	..	..	..	1
Trachoma	..	..	..	..	12	..	..	..	12
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	47(40)	22(17)	6(2)	4(2)	9(8)	3(2)	..	..	91
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Doctor" on Monday, May 23, 1955. Both conferences will be held at 8 p.m. in the Stawell Hall, 145 Macquarie Street, Sydney. Bodies wishing to be represented or persons wishing to attend should notify the Honorary Director of the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BW 7483, BU 5238. Telegraphic address: "Postgrad, Sydney."

Brydon Cup.

The Post-Graduate Committee in Medicine in the University of Sydney wishes to acknowledge the gift of the Federation of Country Local Associations and the Northern District Medical Association of a cup to be known as the "Brydon Cup" to honour the memory of the late Dr. A. G. Brydon, of Urunga, New South Wales, who for many years attended the committee's general revision course and was a regular competitor in the golf competition. The cup will be played for annually during the general revision course and will be awarded to the country member attending the course who obtains the best score in the annual competition for the Post-Graduate Committee in Medicine Cup.

Naval, Military and Air Force.

APPOINTMENTS.

The following appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 68, of November 11, 1954.

Australian Military Forces.

Interim Army.

Royal Australian Army Medical Corps (Medical).

To be Captains (provisionally).—NX700355 Wallace Edward de Launey, 31st March, 1952, and NX700358 Dennis Deane Arnold, 7th April, 1952. NX700355 Captain (provisionally) W. E. de Launey relinquishes the provisional rank of Captain and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (2nd Military District) in the honorary rank of Captain, 16th April, 1952.

Congresses.

INTERNATIONAL CONGRESS OF BIOCHEMISTRY.

The third International Congress of Biochemistry will be held in Brussels, Belgium, from August 1 to 6, 1955, under the auspices of the International Union of Biochemistry. Everyone interested in the broadest aspects of biochemistry is invited to participate in the Congress as an active member. Each active member may introduce his wife or another member of his family as an associate member. The General Secretary is Professor C. Liébecq, 17, Place Delcour, Liège, Belgium.

Australian Medical Board Proceedings.

QUEENSLAND.

The following have been registered, pursuant to the provisions of *The Medical Acts*, 1939-1948, as duly qualified medical practitioners: Carruthers, Raymund Gerrard, M.B., B.S., 1954 (Univ. Sydney); Thorburn, Norman Victor, M.B., B.S., 1954 (Univ. Sydney); Roper, Walter Geoffrey, M.B., B.S., 1953 (Univ. Sydney); Sibthorpe, Gwenyth Eleanor, M.B., B.S., 1946 (Univ. Adelaide), T.D.D. (Cardiff), 1950.

The following additional qualifications have been registered: Squires, John Charles, D.C.P. (London), 1953; Goldman, Naphtali, D.P.M., R.C.P. and S., 1954.

Medical Appointments.

Dr. J. W. Rollison (Director-General of Medical Services) has been appointed deputy chairman of the Institute of Medical and Veterinary Science of South Australia.

Dr. F. R. Hone and Dr. I. B. Jose have been nominated by the Council of the University of Adelaide as members of the Council of the Institute of Medical and Veterinary Science of South Australia.

Deaths.

The following death has been announced:

Alsop.—Herbert Fabian Alsop, on November 24, 1954, at Sydney.

Diary for the Month.

Dec. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Dec. 17.—Queensland Branch, B.M.A.: Council Meeting.
Dec. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
Dec. 21.—New South Wales Branch, B.M.A.: Ethics Committee.

Medical Appointments: Important Notice.

Medical practitioners are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Tasmania: Part-time specialist appointments for the north-west coast of Tasmania.

Editorial Notices.

Manuscripts forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary be stated.

All communications should be addressed to the Editor, The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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